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NUTRITION AND RESISTANCE TO CLIMATIC

STRESS WITH PARTICULAR REFERENCE TO

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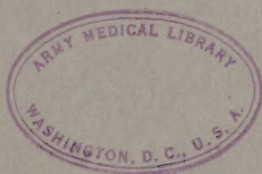
Quartermaster food and container institute for the armed forces

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FOREWORD

Research in the field of human nutrition in relation to environment has produced a volume of literature which has long required authoritative appraisal and critical analysis. For the Armed Forces the problem of the nutritional requirements of men under climatic stress has been particularly acute, for such stress plays an important role in the efficiency, health, and morale of men exposed to extreme climatic conditions.

Therefore, this thorough, painstaking review by Dr. Mitchell and Miss Edman represents a valuable contribution to the planning program of the National Military Establishment. It brings into focus, clearer than ever before, the significant findings on the subject. It describes the current status of our knowledge in regard to (1) the effect of climatic stress on nutrition and (2) the effect of dietary modifications on tolerance to climatic stress. It points out areas which need to be explored further.

In addition to this monograph there was developed under this phase of the project on environment and nutrition, a card index, running to some 4000 items, of the literature on the physiological interrelationship between the animal body and its physical environment. Particular attention was given to covering the literature on man and the relation between diet and stress. Summaries of the articles are included and a full bibliographical reference is given in each instance. The subject matter is conveniently classified for the use of Institute and other workers in this field.

The Food and Container Institute is happy to have supported this study through funds supplied by the Research and Development Branch of the Office of The Quartermaster General. It takes pleasure in presenting what it considers to be a volume of outstanding worth in the field of human nutrition.

Approved for publication

Joseph S. Kujawski, Lt. Col.,QMC
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TABLE OF CONTENTS

Page

RECOMMENDATIONS

The experimental and observational findings presented and discussed in the various sections of this report have established certain facts clearly and certain probabilities that need further exploration. These facts and probabilities relate to (a) effects of climatic stress on nutrient requirements, and (b) effects of dietary modifications on tolerance to climatic stress. Basing judgment upon human experimentation and experiences only, it seems clear that climatic stress may modify greatly the body's requirements for food energy (calories), for water and for salt. It is less certain, though probable, that under conditions of excessive sweating the requirements for iron and for calcium are increased; there is still less assurance that in anoxic anoxia induced by altitude the need for ascorbic acid and for thiamine may be raised.

On the other hand, it can be said confidently that certain dietary modifications increase man's comfort and efficiency under climatic stress, and his ability to tolerate such stress. Carbohydrate and fatty foods are more beneficial than protein foods in combating the damaging effects of cold on heat balance and on the efficiency of neuromuscular and psychomotor performance, while carbohydrate foods are outstanding as compared with both fatty and protein foods in promoting tolerance to altitude, both the anoxic effects and the symptoms of decompression sickness (aeroembolism). The favorable effect of sugar in combating the impairments of vision induced by anoxia are particularly noteworthy. These impairments involve a restriction in the field of peripheral vision and the acuity of vision in dim light. The effect of carbohydrates is quite otherwise in alleviating abdominal gas pains at altitude. For men only moderately active, the specific dynamic action of food is a relatively small item both in withstanding heat and in resisting cold, and becomes even less significant as activity increases. The "glamor nutrients," the vitamins, seem to confer no clearly marked or considerable effects on tolerance to climatic stress when consumed in amounts exceeding the demonstrated requirements in a non-stress environment. A possible exception to the latter statement may be thiamine under conditions of muscular work in severe heat, which may exert a favorable effect on endurance.

The effect on tolerance to environmental stress of the dietary modifications mentioned above was demonstrated generally with diets (or with meals) involving considerable distortions of the usual proportions of carbohydrate, protein and fat. Furthermore, in order to demonstrate the effects more clearly, they were obtained under conditions of incomplete protection by usual procedures against the stress studied; i.e., in the cold experiments the subjects were deliberately underclothed to induce a cold damage, or at altitudes where oxygen inhalation is ordinarily practiced, the subjects inspired ambient air to induce anoxic damage. These are justifiable experimental procedures, but procedures, nevertheless, that modify the practical applicability of the observations secured.

Where climatic factors increase the appetite for those classes of foods shown to be beneficial to tolerance, such as an increased appetite for fatty foods in a cold environment (if such an increase occurs generally), or for sweet foods at altitude, the prescription of appropriate diets for different climates in accordance with experimental findings becomes more feasible.

RECOMMENDED FUTURE WORK OF MILITARY INTEREST. At various places in this report (see pages 15, 38 and 73), it has been noted that animal experimentation has furnished an unsafe guide to human responses to climatic and dietary changes and interactions. Sometimes the laboratory animal fails to respond consistently to dietary supplements that invariably exert a definite response in the human, but more often the laboratory animal responds to a dietary change that is without appreciable effect on the human. Often the results of animal experiments dealing with the same dietary and climatic factors are seemingly confusing and contradictory. Whatever the reasons for these discrepancies, they operate to discount the value of animal experimentation to the problem of the relationship in man of nutrition and climatic stress. However, animal experimentation along these lines, when perfected, will afford valuable contributions to general and comparative physiology and to comparative nutrition. Some problems within the area under discussion may, from their very nature, require animal

experimentation because of the procedures that must be used or the rigors of the controls that must be exercised. But for most problems of this nature, the human subject should be employed and in sufficient numbers to establish the statistical validity of any experimental effects that may be observed.

To the reviewers, the evaluation of human dietaries (military, aviation and naval rations), under either stress or non-stress conditions, by animal experimentation, especially by use of the ubiquitous albino rat, cannot be justified, although it is a not uncommon practice (Williams, 1947). Qualitative, but particularly quantitiative, differences between rat and man in their nutritive requirements militate against the value of such appraisals except where species differences have been shown to be inconsiderable. Under climatic stress, the laboratory animal generally responds so differently, in kind or degree, from the human as to render comparison difficult.

We, therefore, recommend that the problems in the field under discussion to be noted below be studied with human subjects, and that the laboratory animal be used only in "pilot" tests. Furthermore, we agree with Dill (1947) that "Laboratory investigations that concern man in his everyday life, whether at work or at war, require an accompaniment of field studies if they are to have realism and vitality."

Information on the following problems in the relationship of nutrition to climatic stress is needed:

1. The effect on tolerance to intense cold of (a) diminishing the intervals between meals with meals of different character, and (b) inserting snacks of different composition (sugar candy, sandwiches, etc.) between the regular meals. There is reason to believe that such extra meals or snacks, in proportion to their contents of carbohydrate and fat, would exert a favorable effect on tolerance to cold (Mitchell et al. 1946), as well as contribute to an adequate caloric consumption, which is so often difficult to attain under field conditions.

2. The losses of minerals in sweat, and particularly the mineral balances and requirements of calcium and of iron under conditions of profuse sweating (see page 36), need further study.

3. The effects of carbohydrate, fat and protein meals (or snacks) on the tolerance to anoxia under conditions of oxygen inhalation at very low pressures, equivalent to altitudes of 40,000 ft. or more. Are the effects of sugar supplements and oxygen inhalation on tolerance to anoxia additive?

4. The effect of the character of the diet, the distribution of meals, and of dietary supplements, between meals on the rate of acclimatization to heat and to anoxia.

5. The effect of intense heat, intense cold and hypoxia at altitude on preferences for different kinds and classes of foods and for different methods of food processing and preparation. The technic of such tests should be perfected with reference to their physiological aspects and their statistical interpretation (see Henderson, Bean and Ashe, 1945, for example).

6. The relative acuity of the senses of taste and smell under different conditions of climatic stress.

7. The comparative effect on tolerance to cold, to heat and to hypoxia of those diets shown to be most favorable in these climatic situations with those rations in current use in the Army which, in the experience of the OQMG, have proved to be most satisfactory.

8. Fundamental physiological information concerning the effect of diet under conditions of climatic stress on those organs and systems of the body most intimately concerned with tolerance to climatic stress, because of their functions in regulating the heat economy, the body temperature and the transfer of oxygen from the atmosphere to the tissues. These systems are the pulmonary system, the cardiovascular system, the blood, and the skin representing the main area of contact between the body and its environment. The properties of the skin to hold and to release water under climatic variation, to insulate the deep tissues of the body, to protect itself against the damaging effects of direct sunlight and to combat parasitic

invasion (bacterial, fungal and insect), may possibly be influenced by diet.[1]

RECOMMENDED INCLUSION IN ARMY FEEDING PRACTICES OF INFORMATION PERTINENT TO THIS REPORT. Certain facts on the interrelations between diet and climatic stress have been clearly established. Whether these facts warrant modification of Army rations for troops in different climates, or subjected to different climatic stresses, is a matter involving many other considerations. Any increase in the number of standard rations for Army use should offer distinct and considerable advantages over present rations in greater efficiency of Army personnel under the conditions for which they have been designed. The proposed additional rations should be highly acceptable so that their consumption in adequate amounts would be assured. Their packaging, transportation and preservation should be possible in a practical and satisfactory manner.

The advantages of certain types of diets in certain climatic situations have been shown to be distinct, but as compared with prevailing Army rations there is no assurance, from evidence at present available, that these advantages would be considerable. In the field of aviation, the engineering and technological advances in combating bends and anoxia (pressure breathing, pressurized cabins, pre-flight denitrogenation, improved oxygen equipment) are so much more effective than dietary (or menu) modifications as to render the latter of little, if not insignificant, importance in most combat situations.

It is conceivable, however, that certain critical situations may make it advisable, or even imperative, to take advantage of every available expedient to supplement engineering and technological equipment in promoting personnel efficiency. In polar or sub-polar missions, appropriate dietary modifications may reduce to some extent cumbersomeness of the protective clothing that need be worn: in airplane flights at extreme altitudes appropriate pre-flight and in-flight meals may well contribute significantly to operational efficiency, or may reduce significantly the hazard of explosive decompression resulting from combat, when seconds of prolongation of effective consciousness may mean the difference between life and death.

In these situations all available information on the interrelations of diet and climatic stress, as well as the information to be secured from future research, should be valuable to the OQMG in discharging its functions in the Army. It may be put to good use in devising special rations (or meals) for critical situations and in the indoctrination of personnel with regard to on-duty feeding practices.

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[1] Reference might be made here to the studies of Haldi, Giddings and Wynn (1942) on the dietary control of water content of skin, of Edwards and Duntley (1939) on skin pigments, of Mayr (1943) on cutaneous nutrition and metabolism and their influence on the healthy and the diseased skin, of Amersbach et al. (1941) on the effect of vitamin deficiencies, toxic agents and cosmetics on skin respiration, of Radsma and Nizar (1938) on dermal production of lactic acid, and of Burtenshaw (1942) and Cornbleet (1933) on the skin's capacity for self-disinfection.

I. INTRODUCTION

Man inhabits all climatic regions of the Earth, as diverse as those of the polar regions and of the tropics. With the development of the airplane, he has extended to a considerable degree the third dimension of the habitable Earth with its own peculiar climatic features. These facts testify to the great adaptive powers of the human organism. These adaptive powers can be broken down into physiological and constitutional factors on the one hand, and cultural factors on the other.

By reason of purely physiological processes the human body can maintain its temperature within narrow limits under variable environmental conditions simply by modifying its rate of heat production, or by modifying the rate at which heat is dissipated from the surface of the body and from the respiratory tract. Constitutional differences between races of men, such as differences in body size and conformation, differences in pigmentation and other properties of the skin, and differences in the efficiency of temperature regulatory mechanisms may also operate in climatic adaptations.

By cultural methods man can modify his own immediate environment and thus minimize the stress of the climate in which he resides. The type and quality of clothing and of housing and the use of artificial heating, and later cooling, devices enable him to supplement physiological processes and constitutional characteristics in maintaining his normal body temperature in the face of extreme climatic stress.

The diet of men living in different climatic regions varies greatly, both in quantity and in the nature of the foods of which it is composed. These differences are dependent upon the availability of foods of different descriptions, obviously. The prevalence in the diet of the Eskimo of foods high in protein and in fat may be largely due, as Thomas (1927) believes, to the unavailability of carbohydrate foods during most of the year. On the other hand, Burton and associates (1940) have reported that, in a cool environment, human subjects prefer foods of higher caloric value per gram and lower equivalent respiratory quotient, both of which are prominent characteristics of fats, and that appetite plays a significant role in acclimatization to cold. This belief derives a certain measure of circumstantial support from the fact that prevailing diets in hot climates are so often poor in fats and high in carbohydrates (Woodbury, 1942; Nicholls, 1938; Lindstedt, 1938). There is a possibility, therefore, that men to a certain extent select their foods and acquire food habits best adapted to aid them in combating climatic stress.

These possible relationships between diet and tolerance to climate have been studied sporadically and largely upon laboratory animals, for many years. However, during the period of World War II these relationships demanded specific and immediate investigation upon human subjects for the purpose of rationing our service men assigned to different climatic regions in the most effective way. The value of protective clothing in polar and sub-polar regions, or in high-altitude flying, is limited because, first, the protection afforded against intense cold by any reasonable assemblage of clothing is a function of time, i.e., each assemblage of clothing has its "tolerance time" (Newburgh and Harris, 1945). In the second place, an assemblage of clothing reasonably effective in extreme cold is so cumbersome as to impair the efficiency of a man in the performance of such manual operations as the piloting or navigation of an airplane, or the manipulation of a machine gun. If certain dietary modifications would supplement clothing in protecting aviators or ground troops against cold, it may be advisable at certain times to modify Army rations for use in cold climates or cold seasons.

In the tropics another dietary problem arises from the possibility that the extreme sweating induced by the critical need of dissipating body heat at a rapid rate may lead to excessive losses of water-soluble nutrients--vitamins, minerals, and amino acids--necessitating greater supplies in the diet. Temperature and humidity both contribute to the magnitude of these losses, such as they are.

In high-altitude flying, the diminished atmospheric pressure, and in particular the low

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partial pressure of oxygen in the inspired air is a type of climatic stress presenting a serious hazard to the preservation of physiological and psychological efficiency and even of life itself. The maintenance of cabin pressure at ground-level magnitude with normal partial pressure of oxygen is a complete defense against this hazard except in combat or in accident. The breathing of pure oxygen in an airplane cabin not so fortified is effective in combating the anoxic stress up to certain high altitudes. But some supplementary protection such as may be afforded by diet would be of value in such critical situations as bail out, loss of cabin pressure, or failure o. the oxygen system when additional seconds of consciousness can mean the difference between life and death. The proper rationing of mountain troops would be another phase of this problem.

The urgency of these problems bearing on the relationship of diet to climatic stress induced government war agencies, particularly the Office of Scientific Research and Development, to spend many hundreds of thousands of dollars in aiding scientific research in universities and other institutions, directed toward the improvment of Army and Navy rations in varied climates. This report will be concerned with the physiological studies of diet as related to climate. In addition, many biochemical and engineering investigations of food stability and preservation under different conditions of temperature and humidity, and of proper packaging and transportation, were undertaken under the stimulus of the war effort.

Experimental air-conditioned chambers and decompression chambers have been used in most of the investigations to be reviewed in this report, whether the subjects were laboratory animals or men, but the simulation of climatic conditions in such equipment, and in particular the simulation of living conditions in different climates in restricted quarters, is never complete. The diurnal variations in temperature, humidity, air motion and insolation, both direct and indirect, are difficult or impossible to duplicate in an experimental chamber: hence, the necessity of checking laboratory results with actual field tests, before practical conclusions can be drawn. In these checks, questions of food habits of men and of the acceptability of proposed dietary measures are of the greatest importance.

The information secured from the many experimental explorations into this, until recently, largely unexplored area of diet in relation to climate may be divided first into the various types of climate, characteristic of the arctic and antarctic regions, the tropics, and high altitude, and then two distinct divisions, one dealing with the effect of climate on dietary requirements, and the other dealing with the effect of diet on tolerance to climatic stress. The dietary modifications that will be considered under the latter heading will be modifications of an already adequate diet as this term is ordinarily used. Obviously, a diet inadequate in one or more nutrients can be improved for use in any climate by correcting its deficiencies.

The literature coverage bearing directly on the relationship of diet to climatic stress should be fairly complete and has been supplemented by access to unpublished reports of various research agencies concerned with this subject especially during the period of the late war. The various sections of the report include also short discussions of the physiological effects of the climatic factors considered. The literature citations here are admittedly incomplete and have been selected for special reasons from a much more complete file. Only those physiological responses to climatic stress have been considered that bear some relationship, direct or remote, to nutrient requirements or nutritional processes.

II. Diet In A Cold Environment

The Physiological Effects Of Cold

One might expect that the physiological effects of cold would be directed toward an increase in the metabolic rate, through voluntary or involuntary action, and to a decrease in heat loss from the surfaces of the body through postural and vasomotor adjustments.

1. BASAL METABOLISM. Observations on the metabolism of the laboratory rat after previous exposure to cold have revealed a marked stimulation when the measurements are made under basal conditions (see, for instance, Benedict and MacLeod, 1929). However, Treichler and Mitchell (1941) found that this elevation in basal metabolism following cold exposure was exhibited only when the caloric intake of the rat was increased in response to the increase in caloric requirements. Hence, the increase in basal metabolism is a direct dietary effect, and only indirectly an effect of a cold environment. Similarly, the elevated metabolism of the Eskimo reported by Krogh and Krogh (1914-15), by Heinbecker (1928) and by Crile and Quiring (1939), is probably the direct result of a high-protein dietary (Heinbecker, 1931), not of cold per se.

2. THE COLD STIMULUS TO METABOLISM. During exposure to cold, the metabolism of animals is increased independent of voluntary muscular activity so that the "resting" metabolism may amount to 4 times the basal rate (Giaja, 1925), or as much as 5 times in man during shivering (Adolph and Molnar, 1946). In a moderately cold environment, the metabolic stimulus is more potent on the sleeping than on the waking subject (Stillman and Lawrence, 1925). According to Burton and Bronk (1937) and Spealman (1945a), shivering occurs when the rectal temperature descends to some critical level, perhaps characteristic of the individual. Apparently an increase in metabolism induced by cold, unaccompanied by increase in muscle tonus or by shivering, does not occur to any considerable extent, and is not an important item in the body's protection against cold (Hemingway and Hathaway, 1941). Whether "chemical regulation" of body temperature in the Rubner sense of the term actually exists, cannot be decided from the results of experiments in which variation in muscle tone is not accurately measured. Glickman (see Keeton and Mitchell, 1944, p. 36 and chart 2) has found a correlation of +0.930 ± 0.012 between the heat production of human subjects exposed to cold and the action potential of the muscles for a range in heat production from 43 to 108 cals. per m^2 per hour. The regression of one variable on the other was linear and the fact that the linear relationship extended down to metabolic rates approximately basal in magnitude would lend support to the belief that the elevation in heat production brought about by cold is traceable to the contractile function of the muscles.

The metabolic mixture from which the energy resulting from cold stimulus is derived, even when shivering supervenes, is the same as that prevailing before cold exposure. This conclusion of Swift (1932) was based upon careful measurements of the respiratory quotients of human subjects, with due regard for the disturbing effects on this quotient of the change in respiration that may follow exposure to cold. The very low R.Q.'s that have been reported for the dog in a conditon of extreme hypothermia (Finney, Dworkin and Cassidy, 1927) obviously do not possess a simple metabolic interpretation. The changes in blood sugar level on cold exposure do not seem to be consistent: in the report of Keeton and Mitchell (1944) no considerable or consistent effect was observed, although Leonhardt (1941) noted a distinctly increased level on the local application of cold. In the chicken, hypothermia may result in a lowering of blood sugar (Rodbard, 1947).

The physiological response to the cold stimulus is evidently mediated through the thyroid glands (Ring, 1942; Starr and Roskelley, 1940; and Leblond et al., 1944), the adrenals (Britton, 1928) and the pituitary (Tyslowitz and Astwood, 1942). Dorfman, Horwitt and Fish (1942) have established the presence in human urine of a cortin-like substance capable of prolonging the life of adrenalectomized rats exposed to cold. This substance may be a cortical steroid (Dorfman et al., 1946). Cold exposure regularly increases the urinary output of 17-ketosteroids in normal men (Freeman, Pincus and Glover, 1944).

3. LOWER LIMITS OF TOLERABLE TEMPERATURE. The minimum temperature to which the body of homeotherms may be reduced by severe exposure to cold, especially immersion in cold water, and still permit recovery in the large majority of cases on rewarming has been placed at 77° F. for the rabbit by Jackson and Alonge (1934), and at about 78° F. for the dog by Woodruff (1941). From records of shipwreck survivors in the Bureau of Medicine and Surgery of the U. S. Navy, Molnar (1946) concluded that probably no man immersed in water can survive a rectal temperature of 75° F. (see also Scheiniss, 1943; and Spealman, 1946). Obviously, a time factor should be involved in any such estimates. The increase in metabolic rate induced by cold may reach a peak of 6 times the basal, but when the body temperature falls, the heat production also falls until at rectal temperatures of 80° to 85° F., the metabolic rate is about basal in magnitude according to Molnar.

4. SWEAT SECRETION. Although sweating is not ordinarily associated in one's mind with a cold environment, it becomes a serious problem when men in arctic clothing are required to perform considerable muscular work. Siple (1945) has discussed this situation from the standpoint of clothing, and the great importance of "under dressing" during periods of muscular activity in order to avoid accumulation of sweat in the clothing. According to Siple "there are two natural boundaries which limit the extreme rate at which the body can be cooled. The first is when cooling exceeds 1200 calories, causing human flesh to freeze upon exposure....The second boundary is when the air temperature drops to between -50° and -60° F. Then exercise no greater than fast walking, creating deep breathing, may cause hemorrhage in the bronchial tubes."

The subject is further considered by Belding, Russell, Darling and Folk (1947a, 1947b). Sweating is shown to be an inefficient way of body cooling when men are heavily dressed in the cold, because much of the sweat evaporated from the skin is condensed in the outer layers of clothing. The amount of heat thus recontributed is proportional to the ratio of the amount of insulation lying outside the point of condensation to the total insulation. In subsequent periods of inactivity this condensed moisture impairs the insulating capacity of the clothing. For men wearing the Arctic Uniform and exposed to a temperature of 0° F., the moisture loss from the body is all "insensible perspiration" until the rate of energy production is equivalent to about 175 cals./m^2/hr. (3.7 met)[1]. Thermal sweating appears as energy production rises from 3.7 met to 5.0 met, while from the latter point to one of 8.0 met, the relationship is a linear one. At 8.0 met, the sweat production may amount to 1000 gms. per hour. The water-soluble nutrients that are lost in this water output will be considered in a later section entitled "Diet in a Hot Envireonment."

5. GASTRIC EVACUATION TIME. In dogs a cooling environment decreases the gastric emptying time, according to the observations of Sleeth and Van Liere (1937) and of Olevskiĭ, Zelenko and Kuz'menko (1936). According to the former observers "this work gives experimental evidence for the basis of the recognized fact that an individual often feels more hungry during cold weather and less hungry in extremely warm weather." But whether these observations apply to man is doubtful in view of the report of Henschel, Taylor and Keys (1944) that an elevated environmental temperature will generally (16 of 17 subjects) decrease the gastric emptying time in man, while in the dog a hot environment will prolong gastric evacuation (Sleeth and Van Liere, 1937).

6. THE PATHOLOGY OF COLD. Horvath and Freedman (1947) studied the influence of cold upon the efficiency of men. The reaction time to visual stimuli was not altered during continuous exposure to low temperatures for eight to fourteen days, but in a short time the dexterity of the fingers and hand strength were markedly diminished. Muscular fatigue (Giaja, 1932) and nutritional anemia (Manville and Chase, 1937) impair resistance to cold.

The pathology of cold exposure is discussed by Freedman (1946), Schneider (1946), and Talbott (1944a). Attention may also be called to the book by Luyet and Gehenio (1940): "The Mechanism of Injury and Death by Low Temperatures."

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[1] 1 met (Gagge, Burton and Bazett, 1941) is equivalent to a metabolic rate of 50 cals./m^2/hr., the metabolism of a resting subject in a sitting position.

The Effect of Cold on Nutrient Requirements: Animal Experiments.

1. ENERGY REQUIREMENTS. The energy requirements of animals are increased in response to a cold environment in proportion to the increase in metabolic rate. The zone of thermal neutrality, within which temperature exerts no stimulating effect, is shifted downward in the temperature scale as the metabolic rate is increased by muscular activity or the ingestion of food. In animal husbandry practice, it has been well established (see citations from Black and Swift, 1943) that fattening steers and well-fed dairy cows produce as economically from the standpoint of feed costs, when housed in an open shed, with protection only from wind and rain, as in a heated barn. In a laboratory experiment, Swift (1944) showed that the critical temperature of the fasting mature albino rat is lowered 1^0 C. by the consumption of a high-protein diet in amounts to maintain body weight. In animals with a greater specific dynamic action of food, the depression of the critical temperature by feeding would be expected to be greater.

Herrington (1940) has reported observations on the rate of increase in the metabolism of small laboratory animals at temperatures below the critical, in the fasting condition and with activity restricted only by the small size of the cages. Below the critical temperature the relationship between metabolic rate and temperature was linear for mice, rats and guinea pigs, and the increments in metabolism per m^2 per 24 hours per 1^0 C. drop in environmental temperature were 46.3, 43.2 and 26.1 cals. for mice, rats, and guinea pigs, respectively. It may be computed that the increase in the fasting resting metabolism per m^2 body surface per day per ^{0} C. drop in environmental temperature is 51.3 cals. for a mature pig (Capstick and Wood, 1922) and 24.6 cals. for the mature hen with winter feathering (Mitchell and Haines, 1927), assuming the applicability of Newton's law of cooling bodies to the animal at its critical temperature.

2. VITAMINS. Some recently reported experiments on rats and guinea pigs indicate that cold exposure of these animals may modify their requirements for ascorbic acid. With rats, animals able to synthesize ascorbic acid, Dugal and Thérien (1947) observed a large increase in the ascorbic acid contents of certain tissues (kidneys, liver and testes) on prolonged exposure to temperatures of $+4^0$ to -4^0 C., if the animals adapted themselves well to the changed environment; otherwise, a decrease occurred. If the rats adapted to the low temperatures received daily supplements of ascorbic acid, the increases in tissue ascorbic acid were much smaller. These results were confirmed with guinea pigs, animals unable to synthesize ascorbic acid, in that resistance and adaptation to a cold environment ($+8^0$ C. to -8^0 C.) depended on the amount of ascorbic acid received daily in the diet, which was varied from 0.5 mg. to 75 mg. Adaptation to cold was measured by body weight changes and improved even up to the highest vitamin dosage.

The observations of Grab and Lang (1946) concerning also the problem of the relation of ascorbic acid to cold resistance, bear a different interpretation. Working with guinea pigs, their plan involved feeding three groups of animals, on diets differing only in their contents of ascorbic acid, for 4 weeks ad libitum in a room at 20^0 C.; they were then exposed to 0^0 C. until death. The levels of ascorbic acid tested were 3 and 30 mg. daily. The daily loss of weight and the survival time were significantly less for the animals receiving no ascorbic acid than for the other groups, but increasing the daily ascorbic acid supplement from 3 to 30 mg. brought about no significant improvement in resistance to cold. In these experiments, ascorbic acid was a factor in cold tolerance only to the extent that it was needed to cover the requirement at moderate temperatures, there being no indication that cold exposure increases this requirement. In these experiments the loss in body weight during the period of cold exposure was correlated with the survival time. In the authors' opinion a low rate of weight loss means a relative inability to draw upon tissue reserves for energy to meet the increased requirements of a cold environment.

A similar experiment by the same authors (1944) showed that a dietary deficiency of vitamin A or of vitamin B_1 impaired the resistance of rats to cold. The effect again did not seem to depend upon some intrinsic property of the vitamins, but upon the ability to draw upon energy reserves in the tissues.

3. PROTEINS. An earlier study by Lang and Grab (1944) on growing rats, indicated,

5

though not too surely statistically, that inadequate levels of dietary protein (6 and 9 percent of the dietary energy) were less favorable to cold resistance than more nearly adequate levels (12 and 15 percent of the dietary energy). The plan of the experiment was similar to their ascorbic acid work.

The Effect of Cold on Nutrient Requirements: Experiments on Human Subjects.

1. ENERGY REQUIREMENTS. The basal metabolic rate of the nude human body increases as the environmental temperature drops below the critical (Hardy and Soderstrom, 1938), the increase being linear. But this relationship has little significance in practical nutrition, because the human animal protects himself against his environment by wearing clothing and varying his clothing with changes in his environment. The seasonal variation in basal metabolism of clothed women in a temperate climate is inconsiderable (within a range of 15 percent), with the lowest average values in the winter rather than in the summer (Gustafson and Benedict, 1928).

The effect of extremes of climate on the total caloric requirements of man has not been studied in a quantitative fashion until the late war. In 1946 Dill, Johnson and Kark prepared a critical review of the nutrition of United States and Canadian soldiers stationed in climates ranging from the arctic to the tropics. For the purpose of comparing diets in different climates (Johnson and Kark, 1947), data were selected only from groups of men receiving ample rations of wide variety and of such quantity that more could have been eaten if desired. In these selected data, a striking correlation is evident between the average voluntary caloric intake and the mean environmental temperature to which the groups of men were exposed. The range in caloric intake was from 3100 cals. daily in the desert (mean temperature, 92° F.) to 4900 cals. daily in the Arctic (-30° F.). The regression of daily caloric intake on mean environmental temperature was 15.5 cals. per ° F. change in temperature.

According to the authors of the report: "This very large difference in caloric intake cannot be explained in terms of changing basal metabolic rates (DuBois, 1936), which vary at the most by 20 pct. between arctic (Greenland) and tropical (Java) environments (equivalent to only 400 calories/24 hours); nor can it be explained in terms of difference in body size (Table 1) or in terms of different activities, since the ground troops carried out much the same tasks in all environments. We have no crucial evidence to decide this latter point, but we believe that the caloric expenditure for a given task is greater in cold than in warm climates because of the hobbling effect of arctic clothing and equipment. In addition more heat is required in cold than in warm environments to maintain thermal equilibrium."

In a later report, Gray, Consolazio and Kark (1947) present direct experimental evidence of the effect of clothing on caloric requirements. In these experiments 5 young healthy men performed the same amount of muscular work (pedalling a bicycle ergometer and clearing an obstacle) at three different temperatures (-16°, 59° and 93° F.), wearing appropriate uniforms in each environment and, as a control, the same uniform in each environment. The caloric output for a given amount of work performed was determined. The data secured lead the authors to conclude: "The change in metabolism due to the hobbling effect of clothing appears to be at least twice as great as the change due to ambient temperature and must be regarded as playing a major role in the increased caloric requirement as the temperature is lowered..." The hobbling effect of clothing may be even greater than this, since when clothing is adapted to environment the work may conceivably have been carried out more efficiently than when no such adaptation is made, and the heat production stimulated less at the extreme environments.

The significance of the correlations observed by Johnson and Kark (1947) between ambient temperatures and caloric requirements is somewhat obscured, though not destroyed, by the fact that the average body weight of the men in the coldest climate is about 8 kgm. heavier than that of the men in the hottest climate.

The great importance of maintaining an adequate caloric intake of men in polar and subpolar regions is emphasized by the field tests on military personnel reported by Kark, McCreary, Johnson, Melson and Richardson (1944). A ration of high acceptability is indicated in such cases. It may be interpolated here that the evils of over-weight and over-eating that over-burden the heart and shorten the life in a temperate climate may be mitigated in a cold

climate by the extra insulation afforded by a thicker layer of subcutaneous fat.

2. WATER AND SALT REQUIREMENTS. Besides the effect of cold on the energy require-
ments of man, there is an effect upon water requirements insofar as the vaporization of
water from skin and lungs is diminished and, in both water and salt requirements, insofar
as the activity of the sweat glands may be suppressed or stimulated. The estimate of Adolph
(1933) that in temperate climates the water requirement of man approximates 1 cc. per ca-
lorie of heat produced' is evidently not applicable to an arctic environment.

The Effect of Diet on Tolerance to Cold: Animal Experiments.

1. FAT, CARBOHYDRATES AND PROTEINS. Experimental study of a possible relation-
ship between the nature of the food supply, with reference to the three main classes of or-
ganic nutrients, and tolerance to cold seems to have been largely undertaken with laboratory
animals, until recently at least. Leblond, Dugal and Thérien (1944) noted the free-choice
selection of proteins, carbohydrates and fats made by nearly mature albino rats when exposed
to a temperature of -2° C. It was observed with only six experimental animals, however, that
the more fat and the less carbohydrates voluntarily consumed, the higher was the tolerance to
cold as measured by body weight changes and survival time. The relative intake of protein
seemed immaterial provided a certain minimum proportion was consumed. In experiments
on large numbers of rats, Dugal (1944) observed that the consumption of a diet high in fat was
associated with distinctly lower mortality rates in the cold (-1° C.) than was that of a diet
containing a lower proportion of fat. In control rats maintained at comfortable temperatures,
the two diets were equally satisfactory. In a later report to which reference has already been
made, Dugal and Thérien (1947). present evidence that seems to confirm the obvious inter-
pretation of the previous experiments, that dietary fat is much more beneficial than carbo-
hydrate in promoting survival in the cold. The observation is reported that in rats the
increase in ascorbic acid content of the tissues is smaller with a diet rich in fat than with a
diet rich in carbohydrate. The situation may be interpreted to mean that the more difficulty
the rat experiences in surviving intense cold, or in adapting to it, the greater is the increase
of ascorbic acid in its tissues.

The uncertainty that seems to be inherent in the interpretation of the results of feeding
experiments on animals in which the experimental diets are allowed ad libitum is illustrated
by a comparison of the results secured by Leblond, Dugal and Thérien (1944) with rats and
those of Donhoffer and Vonotsky (1947a) with mice. The purposes of the two experiments
were the same, namely, to study the effect of environmental temperature on food selection.
The technics were not the same, in that in the Canadian experiments the proteins, carbohy-
drates and fats were offered separately, while in the Hungarian experiments the mice were
allowed their choice of three diets, each containing one-third of a standard mixture and two-
thirds of either starch, casein or lard. In the Canadian experiments the animals preferred
fat in securing extra food energy in the cold, while in the Hungarian experiments they obtained
their extra calories exclusively from starch, after a transient initial preference for fat. A
more intensely cold environment was selected for tests in the Canadian (-2° C.) than in the
Hungarian (10-11° C.) investigations, and the control temperatures were similarly related,
i.e., "normal" room temperature and 29-33° C. In both cases the energy requirements and
the caloric intake were markedly increased at the lower temperature. The interpretation in
the one case, supported by independent evidence, is that rats select fatty foods in a cold en-
vironment because thermal equilibrium can be maintained better on fatty than on carbohy-
drate or protein foods. In the other case, the authors are more conservative, merely offer-
ing the suggestion that this change in appetite is due to a regulation set in motion by changes
in external temperature and probably mediated through the thyroid gland (Donhoffer and
Vonotsky, 1947b). In unpublished experiments from Keeton's laboratory, no consistent effect
of a change in environmental temperature from ordinary room temperature to 2° C. on the
free selection of protein, carbohydrate and fat was noted with adult albino rats.

The investigations of Giaja and Gelineo (1934) were concerned with observations on the
survival times of rats in the cold when fasting and when offered individual nutrients. Proteins
afforded practically no protection over no food at all. Fat was considerably better in this re-
spect, but carbohydrate gave the best average survival time of all. Within the zone of thermal
neutrality, these differences did not appear. The body weight losses of the different groups
of rats were directly correlated with the survival times. The ability to survive seems to de-

7

pend on the ability to metabolize body tissues for the production of heat. Unfortunately for the complete interpretation of these experiments, the food intakes of the experimental rats are not reported.

Another approach to the same problem has been referred to earlier, i.e., to observe changes in the metabolic mixture undergoing oxidation in the tissues, induced by exposure to cold. These changes are revealed presumably by changes in the respiratory quotient or by changes in tissue composition. However, evidence of this type is confusing. Kayser (1937) observed in the guinea pig a decrease in R.Q. on cold exposure, indicating a preferential combustion of fat; Herrington (1940) observed no effect of environmental temperature on the R.Q. of mice, rats and guinea pigs; working with the rat, Samaras (1939), from observation on changes in tissue composition, emphasized the importance of carbohydrate in combating the stress of immersion in cold water, especially the initial stress; the report of Cohn and Gessler (1925) indicates the nonparticipation of protein in the enhanced metabolism of dogs induced by cold. The latter conclusion is opposed to the finding of creatinuria by Samaras in his rat experiments, unaccompanied by an increase in urinary creatinine.

The reported effect of dietary fat on the thyroid gland, a gland that seems to be involved in the enhanced metabolism brought about by cold, is pertinent to this discussion. The Mellanbys (1921) working with puppies; McCarrison (1922) and McCarrison and Madhava (1932) experimenting with birds, reported hyperplasia of the gland when the diet contained fat, particularly butterfat or oleic acid. The results were not confirmed by Remington (1938) in experiments on the rat, either on an adequate or on an iodine-deficient diet. (The prolonged administration of thyroxine to mice greatly increased food intake (Donhoffer and Vonotsky, 1947b) which was furnished, free selection provided, mainly, in many cases entirely, by the extra consumption of starchy foods.)

The importance of fat in the proper nutrition of the skin was revealed by the observation of Williamson (1941) that rats on a fat-free diet developed an abnormal skin, the stratum granulosum becoming especially distinct and the horny layer thick. As the area of contact with the environment, the skin is an important tissue in mitigating the effects of climatic stress. Its response in structure and composition to dietary modifications is worthy of much additional study.

2. VITAMINS. György (1938) has called attention to the earlier appearance in rats of acrodynia induced by pyridoxine deficiency in a cold room at 40° F. than at normal temperatures. In particular he points out the striking similarity between this disease in the rat and the syndrome of chilblain in man, suggesting to him that susceptibility to chilblain may be a function of pyridoxine reserves in the body, and that pyridoxine medication may be of value in the prevention of chilblain. In much the same vein, Champy and Coujard (1940) associates thiamine and frostbite, in that symptoms resembling frostbite may be produced in thiamine-deficient, but not in normal, pigeons by immersing the feet in cold water. Maycock (1943), however, could not detect in rats any favorable effect of thiamine administration on survival after cold shock, or recovery from this condition.

The Effect of Diet on Tolerance to Cold: Experiments and Observations on Human Subjects

1. FATS, PROTEINS AND CARBOHYDRATES: FREQUENCY OF MEALS. The experiments above reviewed suggest strongly that the character of the diet, as well as the amount consumed, may determine to some extent the capacity of the animal organism to resist the damaging effect of cold. In particular, the superior effect of fat and of carbohydrate food over protein food is rather clearly indicated. Whether the same distinction exists among the main classes of organic nutrients in human nutrition will be considered first on the basis of uncontrolled observations of the food habits of human populations.

While scouting the common belief "that people like fat in cold weather and dislike it in hot" in his Arctic Manual (1944a), Stefansson (1944b) summarizes the experience of arctic explorers on this point as follows: "We find, on an exclusively carnivorous diet, that if you derive less than 60 pct. of your calories from fat you begin to have a feeling of dissatisfaction; when you derive only 20 pct. or 30 pct. of the calories from fat you are constantly uncomfortable. There is in the northern woods a term 'rabbit starvation' which refers to a sickness and sometimes death, which results from an attempt to get along on lean without fat." The

advantages and disadvantages in the arctic diet of a high-fat food, "pemmican," first pre-
pared by the North American Indian, have been debated by Stefansson (1944c) in the affirma-
tive, and Johnson, Consolazio, and Robinson (1944), Kark, Johnson and Lewis (1945), and Lock-
hart (1945) in the negative, though they are not talking about the same article of diet except in
name. Lockhart summarizes concisely the basic requirements for a trail ration in the Ant-
arctic: lightness, high energy value, stability, nutritive value, tastiness and simplicity. Non-
fragility and proper packaging are emphasized. An increased proportion of fat calories is
recommended, not on nutritional grounds "but because observations on diets consumed in cold
climates indicate that a larger quantity of fat can be consumed with no deleterious effect..."

Frazier (1945) writes as follows from the experience of the United States Antarctic
Service Expedition of 1939-41: "Individuals who had an abhorrence of fats at home would eat
butter and fat meats in great quantities." Skarland (personal communication), Professor of
Anthropology at the University of Alaska, from admittedly uncontrolled observations in Alas-
ka, states: "As far as white people and other recent arrivals in the Arctic are concerned I
am convinced that the cold environment modifies the food habits to a great extent. People
living out of doors under sub-zero temperatures almost invariably develop a strong 'fat hun-
ger', 'meat hunger', or 'candy hunger.' The only way to satisfy this in the Arctic is to eat
more fat food of animal origin, although fats of vegetable origin might serve as well. Vege-
tarians have difficulties under field conditions, although they can do quite well in the towns
where imported foods are available." However, "People who have recently arrived from
warmer climates have about the same resistance to cold as those who have lived for years in
northern regions." In a temperate climate, a high-fat diet (71 percent of calories) is not well
tolerated and possesses many disadvantages (Consolazio and Forbes, 1946).

According to Corcoran and Rabinowitch (1937), the Canadian eastern arctic Eskimos,
consuming large amounts of meat and fat, possess not only a very active but also an unusual
mechanism for utilization of fats, characterized by low levels of total lipids in the blood, a
high ratio of phospholipids to total cholesterol and low cholesterol values, after the ingestion
of 200 ml. of soybean oil. The absence of ketosis was also noted as unusual.

On the other hand, Johnson and Kark (1947), in their survey of the voluntary food con-
sumption of United States and Canadian troops stationed in widely different climatic regions,
showed that regardless of environment the proportions of food calories derived from pro-
teins, fats and carbohydrates were much the same. Certainly there was no tendency for these
men to consume more food energy as fat in arctic and subarctic regions than in temperate
regions.

An experimental approach to the problem of the effect of dietary modifications on man's
tolerance to cold was carried out during the war in the Research and Educational Hospital of
the University of Illinois in Chicago by a group of investigators headed by Keeton. The ex-
periments were based upon the probability revealed by the investigations on laboratory ani-
mals above reviewed, that the character of the diet may determine to some extent the capac-
ity of the animal organism to resist the detrimental effects of cold. It seemed important to
explore this relationship further with human subjects, having in mind particularly the needs
of military aviation. The effects on cold tolerance as measured by various physiological,
psychomotor and intellective performance tests, of modifications in the proportions of pro-
tein, fat and carbohydrate in the diet, were studied on groups of 10 or 12 young healthy men;
they were conscientious objectors to military service who volunteered as subjects. The men
were clothed in arctic clothing obtained mostly from the Office of the Quartermaster General,
U. S. Army, but in most of the experiments the clothing purposely was planned not to protect
the men completely from cold throughout the exposure period, since it was essential to the
purpose of the experiment that thermal equilibrium be not maintained. The men were ex-
posed for 8 hours daily, 5 days a week, and 4 hours on Saturday, when the experiments were
well under way, to a temperature of -20° F., with minimal air motion. The activity of the
men was restricted by the size of the experimental chamber, and provision made for exer-
cising was rarely used. The experimental diets were consumed in amounts per day required
to maintain body weight and were generally divided into 4 meals a day, one just prior to ex-
posure, one during the exposure period, one on leaving the experimental chamber, and one
just before retiring.

The first experiment by Keeton et al. (1946) was concerned with a comparison of a high-

protein (305 gms. per 3000 calories) with a high-carbohydrate, moderate protein (79 gms. per 3000 calories) diet, the fat content of both diets remaining approximately the same, about 135 gms. per 3000 cals. The food energy required to maintain body weight was considerably less (15 percent) on the high-protein than on the high-carbohydrate diet, but the protection afforded against cold was definitely greater for the latter diet: thermal balance was more nearly maintained, as was psychomotor performance. The superiority of the high-carbohydrate diet in preventing impairment of psychomotor performance during exposure to cold was greater in the "full-clothing" than in the "light-clothing" tests; with reference to the maintenance of rectal and mean skin temperature, the superiority of the high-carbohydrate diet was greater in the "light-clothing" tests. The differences in protective action of the diets was more evident in 4 hour exposure periods than in 8 hour exposure periods, i.e., the men on the high-carbohydrate diet exhibited smaller average drop in rectal temperature by 0.74° C. during 4 hours exposure than the men on the high-protein diet, but during 8 hours exposure the difference in decrement was only 0.58° C. With reference to decrement in mean skin temperatures, the average diet differences (favoring the high-carbohydrate diet) were 2.53° C. in 4 hours, and 1.56° C. in 8 hours.

There was an average 36 percent decrement in psychomotor performance during 8 hours exposure to cold on the high-protein diet, but only 15 percent decrement on the high-carbohydrate diet in the full-clothing tests.

The authors conclude from these experiments: "The superiority of a high-carbohydrate diet over a high-protein diet in increasing the tolerance to cold...under conditions in which the caloric requirements are just satisfied is associated with, and probably causally related to an increased requirement of food energy and presumably an increased heat production of the man. It is not related to the differential specific dynamic effects of the diets as revealed during a six hour period post prandium."

The latter point will be considered further later. In practical nutrition, these advantages of the high-carbohydrate over the high-protein diet must be evaluated in connection with the large difference in diet composition, amounting to some 220 gms. of protein and of carbohydrate per 3000 calories.

To the reviewers it seems probable that the differences in caloric intake between the two diet groups in this experiment can account for only a part, and possibly a small part, of the differences observed in tolerance to cold. Conceivably, the high-protein diet may have depressed muscular activity either voluntary or involuntary (increased muscle tension, shivering) or both. Possibly the maintenance of the glycogen stores in the liver is an important item in cold resistance (Fuhrman and Crismon, 1947). Burton and Murlin (1935) reported a higher heat storage during the second and third hours after a carbohydrate meal than after a meal of meat. Although the authors themselves make no point of this difference, a statistical analysis of the data reveals that the probability that random factors alone were responsible for the observed difference is less than 0.01, and may fairly be neglected.

In the second report (Mitchell et al., 1946) of the Illinois experiments on the tolerance to cold as modified by diet, high-carbohydrate and high-fat diets were compared. Both experimental diets contained approximately the same amount of protein (77 gms.) per 3000 calories, but on the same basis the high-carbohydrate diet contained 374 gms. more of carbohydrate and the high-fat diet 168 gms. more of fat. The food energy required to maintain body weight in the two diet groups averaged less for the high-carbohydrate diet, but the difference was not statistically significant. During the 8 hour exposure periods in this diet comparison either one meal containing 40 percent of the day's calories was served midway in the period, or three meals, each containing 20 percent of the day's calories, were served at 2 hour intervals.

The effect of cold exposure on rectal temperature was smaller on the high-fat than on the high-carbohydrate diet, but only when three meals were served during exposure, the decrements in rectal temperature being, respectively, 0.57° C. and 1.25° C. during 8 hours. The experimental results established a high probability that a high-fat diet is superior to a high-carbohydrate diet in maintaining general psychomotor performance and visual efficiency as measured by critical fusion frequency of flicker ($P = 0.046$), the superiority amounting on the average to about 37 percent. With reference to the speed of tapping, the superiority is

clear-cut (P = 0.022).

Decreasing the interval between meals during cold exposure had no favorable effect on rectal temperature changes if the meals are largely carbohydrate in character, but it has a definitely favorable effect if the meals are largely fat in character (average effect equivalent to a saving of 0.43° C. in rectal temperature, P = 0.00015). The same change in dietary regime progressively and markedly increases the favorable effect of meals on the maintenance of psychomotor functioning, but obliterates entirely the differential effects produced by diets differing widely in their proportions of carbohydrate and of fat. The improvement in performance amounts to about 30 percent, but it cannot be entirely attributed to decreasing the interval between meals, since the caloric intake of the three meals exceeded the caloric intake of the one meal by 50 percent.

In neither this experiment nor the preceding one did the character of the meal consumed just prior to cold exposure exert any appreciable effect on cold tolerance, possibly because the "tolerance time" for the protective clothing extended over the period in which the diet effect would otherwise have been manifested.

The authors of the study just described (Mitchell et al., 1946), conclude: "The superiority of high-fat meals over high-carbohydrate meals in maintaining tissue temperature in a cold environment seems to be related to heat emission rather than to heat production and may involve a temporary deposition of dietary fat in the subdermal tissues following a high-fat meal." This suggestion is based on the work of Schoenheimer and Rittenberg (1935), who traced the distribution in the bodies of mice of dietary fatty acids labeled with deuterium. The experiments indicate that most of the dietary fat is deposited in the fat depots before it is utilized. The fact that a diet difference in decrement in rectal temperature in the cold was demonstrated only when the meals were spaced at 2 hour, rather than 4 or 5 hour, intervals, conforms with this suggestion. The lower the skin temperature of a man in the colder environment, the lower the melting point of the peripheral fats (Schmidt-Nielsen, 1946).

Attention may also be called to the investigations of O'Connor (1942) and of O'Connor and O'Donovan (1942), leading to the suggestion that regulation of body temperature is a consequence of the properties of a monomolecular layer of palmitic and stearic acids on the surface of the oxidation catalyst.

The favorable effect of multiplying the number of meals and decreasing the intervals between meals may be an important factor in protecting men against cold. Haggard and Greenberg (1935) have clearly shown the advantages in physical efficiency and industrial productivity of increasing the frequency of meals.

2. VITAMINS. The third report of the Illinois experiments on diet and cold tolerance (Glickman et al., 1946) was concerned with the effect of high versus low intakes of thiamine, riboflavin, niacin and ascorbic acid. The amounts of these vitamins in the basal diet consumed by all subjects were generally two-thirds, or less, of the recommended allowances of the Food and Nutrition Board of the National Research Council; for the last 3 months of the experiment the quantities per 3000 cals. of diet averaged 33 mg. of ascorbic acid, 1.22 mg. of thiamine, 1.77 mg. of riboflavin and about 11 mg. of niacin. Half of the subjects received by capsule massive doses of these vitamins.

The subjects on the unsupplemented basal diet at no time exhibited clinical symptoms that could be referred to a vitamin deficiency and no biochemical evidence was obtained that the vitamin levels of the basal diet were inadequate for normal nutrition for a period of 3 months. However, a single or a multiple vitamin deficiency in the basal diet definitely impaired the muscular endurance of the subjects in performing a simple manual operation. The addition of the 4 vitamins under study to this basal diet, borderline in its content of the vitamins, produced no evident favorable effects on the maintenance of thermal balance, or of psychomotor or intellective performance during 8 hour exposures to a cooling environment, i.e., -20° F. with considerable protective clothing or 60° F. with little protective clothing. The supplementary vitamin dosages very probably minimized somewhat the fatiguing effects of cold on the retinocortical system as this effect is measured by the critical fusion frequency of flicker.

Observations possessing the same significance have been reported by Blair, Urbush and Reed (1947) on military personnel at Fort Churchill, Canada, who were continually exposed to an arctic environment. In the authors' words: "Limited observations under these conditions failed to show any value of vitamin supplements in the Arctic when the normal diet conforms to the recommended dietary allowances of the National Research Council."

An interesting feature of this experiment (Glickman et al., 1946), in view of the prevailing uncertainty concerning the existence of a true acclimatization to cold (Horvath, Freedman, and Golden, 1947), let alone the mechanism by which it is mediated, is the clear demonstration of acclimatization. After exposure to -20° F. with considerable protective clothing, subsequent exposure to 60° F. with very little protective clothing induced a smaller decrement in rectal temperature than occurred without this pretreatment.

Some study was made by Glickman et al. (1946) of the effect of cold on the excretion of some of the vitamins in the urine. The results demonstrate that exposure to cold increases the excretion in the urine of N^1-methylnicotinamide in proportion to the cold stress applied and to the dietary intake of nicotinic acid or amide. The results suggest that, when the cold stress is sufficiently severe, the output of total nicotinic acid in the urine is definitely, though only slightly, increased, but that cold may actually depress the urinary output of ascorbic acid. The obvious interpretation of these observations is that cold decreases the requirement for nicotinic acid and increases the requirement for ascorbic acid, but until more information is at hand to support the assumption basic to this interpretation that the urinary output of a vitamin under properly controlled conditions is merely a "spill-over" of intake in excess of use, conservatism would be in order.

Greene (1941) in discussing frostbite, trench foot, shelter foot, and immersion foot, lists as possible causes dietary deficiencies of vitamins A, C, and P. The statement is made without any evidential support: "...it is clear that a deficiency of one or other of these vitamins is capable of increasing that exudation from the blood vessels which is the most important damaging factor in frost-bite and trench foot." According to Bordet and others (1941) the vascular disturbances observed after freezing of extremities may be caused by a high content in the diet of ergosterol, ergotamine, choline and acetylcholine.

Thermal Balance in the Cold as Affected by the Specific Dynamic Action of Food: Experiments on Human Subjects

1. GENERAL. It might be expected that the heating effect of food, a phenomenon that has been studied in a quantitative fashion for almost 50 years, would be an item of importance in the maintenance of the thermal balance of the body in a cold environment. That it is an item cannot be doubted, since as much as 15 to 20 percent of the energy contained in a mixed meal may be dissipated from the body as extra heat over the fasting level of production. This extra heat is commonly referred to as the specific dynamic action (SDA) of food, a term originally proposed by Rubner (1902). The production of extra heat is accompanied by a rise in skin temperature (Booth and Strang, 1936), the elevation being smaller for obese than for normal persons.

The magnitude of the specific dynamic action depends upon many factors, known and unknown. The composition of the diet is an important one. Protein alone will raise the heat production of a man over the entire period of its action an amount equivalent to about 33 percent of the contained calories (Krauss and Rettig, 1929). For fat alone, the value is about 5 percent (Murlin, Burton and Barrows, 1936), with carbohydrate occupying an intermediate position.

For mixed meals consisting largely of fat, Benedict and Carpenter (1918) obtained an average SDA of 2 percent of the consumed calories; for a predominantly carbohydrate diet, a value of 6 percent; and for a high-protein diet, one of 12 percent. Essentially the same average results were reported by Wachholder and Franz (1944) on many more subjects. Most of these values are probably minimal because the periods of observation were not sufficiently long to measure the total effect. The specific dynamic effects of the high-protein and high-carbohydrate diets used by Keeton et al. (1946) were determined on 6 subjects each and the total effect estimated by fitting an appropriate equation to the data and extrapolating to the post-absorptive period. The high-protein diet, containing an average of 37 percent of

protein calories, exerted a total SDA of 17 percent of the consumed calories, and the high-carbohydrate diet, one of about 10 percent. These values pertain to meals containing approximately 1000 cals. each. The magnitude of the SDA of food, expressed in this manner, decreases with the size of meal (Wachholder and Franz, 1944), until for breakfasts containing only 222 cals., the SDA is confined to the first hour post-prandium and is almost negligible (Soderstrom, Barr, and DuBois, 1918). In its effect on the magnitude of the SDA, the protein content of the diet is of paramount importance in human nutrition (Jahn and Strössenreuther, 1928).

There is evidence that the basal metabolism and the SDA of protein are inversely related (Baldwin and Shaw, 1938) and that both decrease in old age (Albergo, 1932). Undernourishment seems to affect the SDA of the different nutrients differently (Tsamboulas, 1939). The SDA of protein is not appreciably affected by moderate muscular work (Bahn, 1927).

2. THE ILLINOIS EXPERIMENTS. The most important information concerning the SDA of food with reference to the maintenance of thermal balance, relates to the rate of production of extra heat and the change in rate with time post-prandium. The peak of heat production occurs in the early hours and may reach a height of 40 percent over the basal rate (Kaplan, 1933). The most complete information of this description was obtained by the mathematical analysis of the data on high- and low-protein diets used by Keeton and co-workers (1946); the analysis was made in a paper by Glickman, Mitchell, Lambert and Keeton (1948). The rate of accumulation of extra calories with time post-prandium was found to follow a sigmoid curve with the point of inflection (the point of greatest rate of accumulation) occurring at about 1.5 hours post-prandium for the high-carbohydrate diet, and between 2.0 and 2.5 hours post-prandium for the high-protein diet. The accumulation of extra calories above basal beyond the point of inflection was very well described by the curve of self-inhibiting growth (the law of diminishing returns) as formulated by Brody (1927). Having determined the constants in the equation from the two sets of data differentiation of the equations yielded derived equations from which the rate of extra calorie production can be computed (beyond the point of inflection) for any time post-prandium. The following values, relating to meals containing approximately 1000 cals., were obtained by solving for rate of extra calorie production at even hours (or half hours) post-prandium--

HOURS	EXTRA CALORIES PER HOUR ABOVE BASAL METABOLISM	
post-prandium	High-Protein diet	High-Carbohydrate diet
1.5	--	21
2.0	33	18
2.5	29	16
3.0	26	14
4.0	20	11
5.0	16	8
6.0	12	6
7.0	9	5
8.0	7	3.0
9.0	6	2.3
10.0	4.5	1.8
11.0	3.5	1.4
12.0	2.7	1.0

Above environmental temperatures at which heat emission from the body exceeds heat production in the fasting man, the SDA of food may reasonably be regarded as a wastage of food energy and even as a burden upon the temperature regulating mechanism in a warming environment. Below such temperatures it may serve a useful physiological purpose by sparing body tissues and increasing the tolerance to cold. But in either case it is a small item in the energy economy of man. After a high-protein meal containing approximately 1000 cals., the maximum rate of extra-calorie production for a man weighing 70 kgms. is 33 cals. per hour, attained 2 hours after eating, decreasing in 5 or 6 hours, the usual period between daytime meals, to 16 and 12 cals., respectively, and to less than 3 cals. per hour in 12 hours post-prandium. After high-carbohydrate meals of the same caloric value, the maximum rate is 21 cals. per hour, at 1.5 hours post-prandium, and the rates after 5, 6 and 12 hours are, respectively, 8, 6 and 1.0 cals. per hour. Of the many human activities for which Sher-

man (1945, Table 23) gives the caloric equivalent per hour, there is none, when allowance is made for basal heat expenditure, with as low a caloric equivalent as the SDA, even of a high-protein meal. Thus, the extra calories over basal for standing relaxed are 40 per hour; for hand sewing, 46 per hour; for dressing and undressing, 53 per hour; and for typewriting rapidly, 75 per hour.

The difference in SDA between a high-protein and a low-protein meal of 1000 cals. is even more insignificant, starting at 12 cals. per hour at the peak, and diminishing to 8 and 6 cals per hour, respectively, at 5 and 6 hours post-prandium. It is not surprising, therefore, that Pitts, Consolazio and Johnson (1944) were unable to detect any appreciable increase in the thermal load of men working in a hot environment induced by an intake of 150 gms. of protein daily, as compared with an intake of 75 gms., the caloric intake remaining the same. Also, Keeton and co-workers (1946) found that the higher SDA of a high-protein diet was not the determining factor in the effect upon tolerance to an intensely cold environment of men allowed some freedom of motion. Also, Robinson and Lee (1947), working with domestic animals, did not secure any evidence that a high proportion of protein in the ration had any significant effect upon the reactions of the animals to heat.

3. THE CORNELL EXPERIMENTS. Long (1943) has reported the findings in a rather extensive study on 3 healthy young men, carried out at Cornell University, ostensibly to determine "The effect of the protein level in the diet on resistance to cold with special reference to the gaseous exchange and the reaction of the body thermostat at low temperatures." Since most of the data presented relate to comparisons of heat production in the lying and standing positions, in the post-absorptive state and 1 to 2.5 hours post-prandium, at temperatures ranging from 60° F. to 0° F., and with diets containing from 12 to 30 percent of protein calories, it may be considered essentially a study of the effect of the specific dynamic action of diets of varying protein content on the energy metabolism of inactive subjects at different ambient temperatures. Furthermore, since the metabolism studies "with food" were all conducted from 1 to 2.5 hours after the noon meal, the peak effect of the SDA only was obtained. The two examples of the noon meal given in the report contained approximately 1097 and 1347 cals.

The basal metabolism of the men, measured 16 to 17 hours after food, was not appreciably affected by the protein content of the prevailing diet. The metabolism from 1 to 2.5 hours after food was, of course, markedly higher on the higher protein diets. The SDA of 220 to 255 gms. of protein daily was estimated, from the change in the nitrogen content of the urine in fasting and "with food" tests[2], to be 22 cals. per hour; that for 96 to 104 gms. of protein daily was estimated at 10 cals. per hour., 12 cals. per hour lower. In the inactive state, 12 cals. per hr. may be a considerable item in the energy economy, but with any considerable activity its effect would fade into insignificance. Using the direct determinations of the SDA of high-protein and low-protein meals secured from the data of Keeton et al. (1946), the difference is 12 calories per hour at the peak of heat production, 2 hours after eating, but steadily diminishes to 6 or 7 cals. per hour at the time of the next meal.

The author concludes: "The totality of data on thermal conductivity of body tissues, body heat storage, and heat production suggest that when extra heat was needed by the body for maintenance of vital functions in cold environments, a greater stimulation of the deeper and superficial tissues of the body was obtained from the oxidation of the high-protein meals than was obtained from the oxidation of the low-protein meals. If the tissues, organs, and glands of the body required stimulation at the low temperatures imposed in this research to maintain the temperature of the circulating blood at a normal level, then the extra stimulus obtained from ingesting the larger amount of protein calories in the mixed diet was always available."

This conclusion is well substantiated for inactive men in the fasting state or within 2.5 hours after eating, when the SDA of the food is maximal.

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[2] The method here used to measure the heat increment of dietary protein (Table 70, Long 1943) implies that all of the energy produced from the protein catabolized in the body above the fasting protein catabolized, assessed at 26.51 cals. per gram of extra N in the urine, appears as extra heat and is in fact the heat increment, or specific dynamic action, of the protein.

14

The following conclusion, to which considerable prominence is given in the text of Long's report, is much less obvious: "The experimental evidence obtained in the lying tests at 40° F. indicates that the body protection afforded by the clothing alone may amount to about 35 percent of the total heat increment, resulting from tests in which maximum insulation was combined with high-protein meals. The remainder of the total heat increments (65 percent) may be attributed to the protein stimulus. In view of these determinations, it is belived that during exposure to cold, protein alone contributes something to the physiological comfort of man that is not furnished by clothing or other body insulation alone."

Changes in rectal and skin temperature during several hours of cold exposure, as important indices of the effect of dietary modifications and variable body insulation on the thermal balance, were not made. Such temperature recordings were made during the short metabolism periods (8 to 12 min. duration), but these were considered merely as "secondary indices of effects of dietary and clothing modifications." During the fasting and "with food" tests these indices favored the high-protein meals when the subjects were inactive, but during work on the treadmill, the results of which are only scantily reported and discussed, the temperature differences secured on different dietary regimes are generally insignificant in magnitude and they do not always favor the high-protein diet.

It is unfortunate that more attention was not given to measurements of body temperature changes and changes in physiological and neuromuscular efficiency over considerable periods of time during cold exposure and subsistence on different diets. Such measurements are of primary importance in assessing tolerance to cold; they measure the net response of the body to climatic stress, while changes in metabolic rate measure only the direct effects of diet that appear on only one side of the thermal balance sheet. It may be significant in Long's experiment that "Subjective expressions after ingesting the protein meals were not indicative of the measured metabolism. In basal experiments the sensory expressions corresponded more closely with the measured metabolism."

It seems fair to conclude that the Cornell experiments afford little information on the effect of different levels of dietary protein on resistance of man to cold. They do, however, afford important information of the operation in the cold of the differential specific dynamic actions of diets containing widely different proportions of protein. To demonstrate these comparatively small thermal effects it was necessary to maintain the subjects in a condition of inactivity.

Conclusions.

From the observational and experimental information discussed here, certain definite conclusions seem warranted. Certainly a cold environment, in proportion to its severity, definitely increases the caloric requirements of man. Its effect upon water requirements is one of depression except in so far as sweating may occur during periods of work of a severity of 4 met or more when heavy arctic clothing is worn. The loss of salt, vitamins and minerals in thermal sweat will be considered later.

Diet modifications may definitely affect the tolerance to cold. The Illinois experiments prove definitely that a high-carbohydrate diet, which, as a matter of fact, approximates closely what would be considered a typical American diet, is superior in this respect to one that is top-heavy in its proportion of protein. Whether the observed difference in tolerance-promoting potency between these two diets is due to the difference in protein content or to the difference in carbohydrate content has not been determined. However, the fact that varying reciprocally the proportions of carbohydrate and fat in diets containing adequate but not excessive proportions of protein does not depress the tolerance-promoting effect of the so-called high-carbohydrate diet, is explained on the premise that only protein among the three main classes of organic nutrients exerts such a depressing effect. Dietary fat under some conditions improves still further the relatively beneficial effects of carbohydrate foods. The levels in the diet of thiamine, ascorbic acid, riboflavin and niacin, provided they are present in proportions adequate in a comfortable environment, seem to exert no appreciable effect upon tolerance to cold.

In practical dietetics, it would seem that diets in a severely cold environment are not benefited with reference to effects upon cold tolerance by high intakes of protein. The extra calories required in the cold, as compared with the warm, environment might better be covered by an increased intake of carbohydrate, and particularly fat, foods. The extent to

15

which this recommendation can be put into effect in feeding communities of men will depend upon other than nutritional factors, such as acquired food habits, the expected duration of residence in an arctic climate, the motivation for such residence, and the extent to which the indicated diet can be made acceptable to the palate and maintained acceptable under arctic conditions. To the extent that "fat hunger" develops in men residing in polar and sub-polar regions, the indicated changes from accustomed diets may the more readily be made.

In conditions of inactivity high-protein foods may exert a temporary favorable effect on cold tolerance for a short period after consumption, due to their high specific dynamic action, but under conditions of normal activity they might better be eschewed.

There is some evidence and considerable rational support for the belief that decreasing the intervals between meals, especially if the foods are rich in fat, may increase their favorable effect on the thermal balance in a cold environment. If snacks between regular meals induce a greater caloric consumption, this in itself may be beneficial, but the problem needs further study.

Animal experiments support some of the above conclusions, in particular the neutral or unfavorable effect on cold tolerance of dietary protein, but some of the interpretations of these experiments have not been shown to apply to man, in particular the favorable effect of ascorbic acid. The apparently contradictory results of many of these experiments, indicate either a defective experimental technic that does not control factors that may dominate the outcome, or the existence of differences among animal species in respect to the relationship of nutrition to climatic stress. It seems certain that in this field of research, the information secured from the best controlled animal experiments should not be applied to human dietetics prior to actual field tests. It may even be doubted that animal experimentation in this field of research in human nutrition is a profitable undertaking.

III. DIET IN A HOT ENVIRONMENT

The Physiological Effects Of Heat.

The physiological effects of tropical climatic conditions upon man have been reported extensively by Sundstroem (1926) with special reference to adaptation. The reviews of Machle (1944), of MacPherson and Lee (1945), of Robinson and Gerking (1947), and of Machle and Hatch (1947) may be consulted with profit. We would like to call particular attention to the review of Lee (1940) entitled "A basis for the study of man's reaction to tropical climates." This review is a remarkably complete discussion of the subject, replete with critical evaluations of laboratory evidence. The logical development of his subject has not led Lee into the exposition of those mathematical relationships between the body and its thermal environment that, however complex, seem still to be undue simplifications of the practical situations that develop in the field. As Machle and Hatch state: "Man as a functioning organism is quite different in character than any of the systems into which, in an analytic approach, he may be resolved."

1. EFFECTIVE TEMPERATURE. There is one relationship, with an empirical rather than a rational basis, that has proved most useful especially in evaluating tropical climates. The "effective temperature" scheme was elaborated by Houghton and his co-workers in the Research Laboratories of the American Society of Heating and Ventilating Engineers in Pittsburgh, Pa. (see Houghton and Yaglou, 1923). By exposing human subjects, comfortably clothed, to various conditions of temperature, humidity and air motion, when at rest, those zones within which sensations of comfort, or of equal degrees of warmth and of cold, were delineated. From the results of a very large series of experiments, an empirical nomogram was constructed (Yaglou, 1926; A.S.H.V.E. Guide, 1947), permitting the integration of dry bulb temperature, wet bulb temperature and air motion into a single term, the "effective temperature." The effective temperature (E.T.) may be defined as that temperature of a still, saturated atmosphere that would produce the same senations of warmth or cold as the given combination of dry and wet bulb temperatures and air motion for men at rest and comfortably clothed. Yaglou (1926) has developed an effective temperature nomogram for men at hard work, stripped to the waist.

2. SWEAT SECRETION. The exposure of man to a hot environment induces a series of adaptive responses including, first, those responses aimed at increasing heat loss from the body. These responses include elevation of body and skin temperature, vasodilatation, increased heart rate, water shifts and sweating. Man shares with the Equidae the ability to increase enormously the loss of body heat as the heat of vaporization by the action of sweat glands distributed over large areas of the body surface. This is an emergency mechanism thrown into operation when the heat emission from the body fails to keep pace with its heat production, as in a tropical environment, or when heat production is elevated by muscular activity to the point where heat loss by radiation, conduction, and convection cannot maintain thermal equilibrium.

The precise relationship between the initiation of sweating and body and environmental conditions, and between the rate of sweating and environmental conditions is obscure. It may involve genetic and constitutional characteristics, since all observers have noted wide variations in sweating among different (and normal) individuals in the same environment. The physiology of human perspiration is dealt with in a scholarly manner by Kuno (1934), who distinguishes two types of sweat glands, the apocrine glands in the axillae, the palms of the hand, and the soles of the feet, responding to an emotional stimulus only, and the eccrine glands, located in the other areas of the body (and the axillae) and responding to a thermal stimulus.

Unclothed men, on the average, will begin to experience a degree of sweat secretion associated with sensations of distinct unpleasantness at the following limits of air temperature and relative humidity (Winslow, Herrington and Gagge, 1937):

Temperature °F.	Relative humidity pct. saturation	Effective temperature °F.
89	96	88
92	70	86.2
95	48	84.7
98	30	83.2
101	19	82.5
104	0	82.5

The rates of sweating under extreme conditions of thermal imbalance approximate 4 liters per hour, though a production of 1 liter per hour represents many kinds of work carried out under extreme but tolerable conditions. At the same effective temperatures, a hot dry climate, according to Lee (1940; Lee et al., 1941), is much more of a thermal load than a hot humid climate and induces a greater flow of sweat, at least in acclimatized men (see also Gerking and Robinson, 1946). Molnar et al. (1946), from studies in the California desert and tropical Florida, assess the thermal stress of the desert as being 3 to 4 times greater than in the tropics, due in part to the solar energy impinging on the human body in the desert. Adolph (1938) estimates the maximum radiation impinging upon seated subjects to be 250 kg. cals. per hour, of which about half is reflected and about half absorbed.

In unpublished experiments carried out in the Division of Animal Nutrition at the University of Illinois during the war period, the average hourly secretion of sweat for human subjects, nude or very scantily clothed and at rest in an air-conditioned chamber, was 720 gms. under hot humid conditions (dry bulb 101° F., wet bulb 91° F., effective temperature 93° F.), 414 gms. under hot dry conditions (dry bulb 111° F., wet bulb 76° F., effective temperature 87.3° F.), and only 117 gms. under comfortable conditions (dry bulb 85° F., wet bulb 71° F., effective temperature 77.5° F.). A good share of the latter weight loss is insensible perspiration. The subjects (6 in number) of these experiments, though subjected to heat exposure for 8 hours daily 5 days a week for many consecutive weeks, and 4 hours on Saturdays, could not be said to be as highly acclimatized as residents of Australia with whom Lee worked. Vernon's observations (1923) also do not agree completely with those of Lee in respect to relative rates of sweating in hot dry and hot humid environments.

When men work in a comfortable to warm environment, most of the extra heat produced is dissipated from the body as latent heat of water vapor, the emission of sensible heat being but little elevated (Houghton, et al., 1931). The same investigators have shown that muscular work in a hot environment is associated with a rate of sweat loss greater than the sum of the rates of sweating produced in that environment at rest and that produced by the same work in an environment which just does not cause sweating at rest. This degree of excess sweating varies with conditions and reaches a maximum at moderately high effective temperatures. Lee (1940) also gives an illustration of this interesting phenomenon. According to Lehmann and Sjakáll (1937a), the quantity of sweat lost per minute per kgm. m. of work accomplished rises with rising temperature but is independent of the fluid intake.

3. MUSCULAR ACTIVITY. The adaptive responses to heat stress thus far considered relate to mechanisms for increasing heat dissipation from the body, preeminently the sweating mechanism. A second type of response relates to heat production within the body. Sojourn in a tropical climate depresses the will to do work both mental and physical. Lee (1940) considers this question at some length, with reference to experimental findings and field experiences. In himself he notes "a definite reduction in mental power and speed in the two climates with an average effective temperature of 77° F." (Singapore and Brisbane in summer.)

Concerning the effect of the tropics on muscular activity, Lee concludes: "A review of the evidence, however, suggests that we have three grades of effect--(i.) with very light exercise undertaken spontaneously there is a reduced will to work and reduced activity, a truly adaptive phenomenon; (ii.) with the most severe forms of exercise, critical phenomena intervene more rapidly, resulting in fatigue and reduced total energy expenditure, an occurrence adaptive in result though critical in production; (iii.) with intermediate grades of work, especially those undertaken in response to a demand, there is but little reduction of work

18

capacity and total energy production is not reduced. The latter may even be raised owing to a lowered mechanical efficiency. In this last field there is no adaptative change. The higher the effective temperature, of course, the smaller will become the third category of work-task, and the earlier will critical phenomena make their appearance."

4. BASAL METABOLISM. There is a tremendous literature on the effect of a tropical climate on the basal metabolism, but the conclusions drawn by different investigators as to the relationship between climate and basal metabolic rate are divergent. To mention only a few of the more recent reports on this subject, Hafkesbring and Borgstrom (1926-27), Drinker (1936) and Mason (1934) observed definite decreases in the basal metabolic rate in tropical environments, of the order of magnitude of 10 percent. Camis (1936), on the other hand, observed low metabolic rates generally among individuals who had been under tropical conditions for only a short period of time. With longer residence in the tropics, the basal rate was generally higher than those reported in temperate climates. The observations of Camis are directly contrary to the earlier ones of Knipping (1923), who states from observations on 30 subjects (translation): "In the majority of cases, the basal metabolism is increased during the first weeks of residence in the tropics. On longer residence in the tropics the basal metabolism apparently decreases to the predicted level, and on months or years of residence to significantly lower levels. With European residents of the tropics, Malays and Southern Chinese, the basal metabolism remains at these low levels (-2 to -16 percent)." Knipping also reports percentage values for the specific dynamic effect of food in the tropics and concludes that the effect tends to decrease on long residence in a hot climate. The reported values lend little support to this conclusion, while their significance as measures of the SDA cannot be assessed in the absence of an adequate description of the method by which they were obtained.

With such apparently conflicting evidence before them, reviewers of the literature on basal metabolic rate in the tropics have balanced the evidence as best they could. DeMoura Campos (1937) concludes that the preponderance of evidence favors the conclusion that residence in the tropics, particularly in a hot moist environment, lowers the basal metabolic rate, and that this is a measure of adaptation to conditions impeding the dissipation of heat from the body. Albagli (1939), on the basis of the largest series of basal metabolism measurements ever made in South America, concludes that the basal metabolism of normal, well-nourished individuals is independent of climate, being comparable to the standards in vogue in the United States and Europe.

It is interesting to note that Galvão (1947), from very careful measurements on 65 adult male dogs in Brazil, weighing from 3.4 to 31.3 kgms., reports that, in this tropical climate, the basal metabolism per unit of body weight is more constant than the basal metabolism per unit of body surface. He concludes: "If the Rubner-Richet law is true only in cold climates, it has a true thermic significance and expresses a causal relationship between heat loss through the surface and heat production." There may be some question whether the relative inconstancy of the basal metabolic rates referred to body surface may not have been caused in part by the inaccuracy of estimates of surface area by the Rubner formula (see Cowgill and Drabkin, 1927).

Lee (1940, p. 27) discounts the significance of differences in basal metabolism of men observed in different climates on the ground that they are probably traceable to variations in "adventitious activities," particularly muscle tone. The existence or nonexistence of differences in basal metabolic rates in different climates may also depend upon the environmental temperature at the time the measurement is made. The true "basal" condition, in human physiology at least, is thought of as involving a comfortable environment within the zone of thermic neutrality. For nude subjects, DuBois (1936, p. 191) defines this zone as between 27º and 34.7º C. For men fully dressed, McConnell, Yagloglou and Fulton (1924) obtained minimal metabolic rates between 75º and 83º F. effective temperature. On the other hand, many of the published determinations, perhaps most, were determined at "habitat temperature," to use Benedict's (1938) phrase. Thus, changes that Mason (1944) observed in her basal metabolism as she travelled by ship from San Francisco to India were associated with increasing ambient temperature and humidity. Whether they would have manifested themselves if the measurements had been made within the comfort zone is problematical.

If the body temperature is modified by climate, the basal metabolism would be expected

to change also. Using diathermy to induce hyperpyrexia, Christensen (1933) observed an
average rise in the metabolism of 4 men of 10.8 per cent per ^{O} C. rise in rectal temperature.
A small part of the elevation in metabolism was due to the increased activity of heart, lungs
and glands, according to the author, but the major part was an expression of a heightened
cellular metabolism.

5. APPETITE AND DIGESTION. In Lee's experience (1940), "a marked decrease in
appetite, ofttimes amounting to revulsion from food, occurred. The revulsion passed away
with acclimatization, but at no time could the appetite be said to be at temperate levels."
He believes a certain reduction of appetite can justly be regarded as an adaptive phenomenon:
There will be some slight decrease in heat production. The explanation of the impairment in
appetite in tropical heat is not clear. Among other authors, Borchardt (1930) noted that gas-
tric secretion and motility of both human subjects and experimental animals are decreased in
an artificial tropical climate. The longer retention of food in the stomach would be expected
to induce a less intense appetite for a subsequent meal if not too long delayed, but Henschel,
Taylor and Keys (1944) report that, in all but one of 17 young men under observation, the gas-
tric emptying time was faster at the higher temperatures. Twelve of the subjects exhibited
an average decrease of 30 'percent in the gastric emptying time at 120° F., as compared with
that at 77° F.

6. HYPERTHERMIA. Hyperthermia, experimentally produced, has been reported to
induce certain changes in blood composition that might bear upon nutritive requirements.
In guinea pigs, Dobblestein (1940) observed always a lowering of the ascorbic acid content
of the blood in artificial fever: An increase of 2 to 3.5^O C. in body temperature was associ-
ated with a reduction of ascorbic acid in the blood to a level one-half (or less) of normal.
However, this observation was not confirmed for human subjects by Osborne and Farmer
(1942). Using 17 arthritic patients as subjects, no significant changes in the ascorbic acid
level of the blood resulted on elevation of the temperature of the body to 104° F. and main-
taining it there for 4 hours, using a combination of air-conditioned cabinet and inductotherm.
Aron and others (1946) reported in a study of 92 patients that elevation of the rectal tempera-
ture to 106° F. by physically induced fever was followed by a depression of the vitamin A and
carotene levels in the blood plasma, irrespective of the chemotherapeutic agents given before
or during the period of observation. The authors state: "This behavior of the plasma vita-
min A is, to the best of our knowledge, the first biochemical indicator shown to serve as
measurement of the intensity of the action of physically-induced fever on the human organ-
ism."

If hyperventilation occurs during extreme hyperthermia, the pH of the blood will shift to
the alkaline side, due to loss of CO_2 (Bischoff, Long and Hill, 1931; Danielson et al., 1938).

7. WORK CAPACITY. The total metabolic exchange of men at work in a tropical en-
vironment is not increased over that in a temperate environment (Herxheimer, 1933; Ehris-
mann, 1938), but the capacity for work is less. The physical fitness of RAAF ground crews
serving in the tropics deteriorates slowly according to MacPherson and Lee (1945) as time
in the tropics increases, although in their opinion: "...over-all deterioration, about which
many complain, is highly psychological." Psychomotor efficiency, as measured by time for
accurate gun-laying, is depressed under hot conditions (Lee, Klemm and White, 1945): "Re-
action times at effective temperatures of 83.5^O and 94° F. are significantly longer than those
at 65°-70° F. The increment is 5-12 percent. Within the range of effective temperature, 88-
96° F., when the subject is seated at rest...the reaction time does not undergo any further
increase with rise of temperature, even when physical failure is imminent." Reed (1942)
discusses "tropical neurasthenia," a rather inexact functional nervous syndrome, which is
a recognized disabling disorder of great importance in the tropics. It is associated "....with
defective psychologic adaptations to environment and stresses of life and characterized by
increased fatigability."

Robinson (1942) has presented an interesting illustration of the greater endurance for
muscular work, other things being equal, of a small as compared to a large man, under en-
vironmental conditions that place a severe strain on the heat dissipating mechanisms of the
body. There is no difference in muscular efficiency; the determining factor is the greater
ratio of body surface to body weight in the smaller man, since heat dissipation depends
largely upon skin surface while the extra heat induced by muscular work depends largely on

body weight.

8. ACCLIMATIZATION. Unlike acclimatization to cold, acclimatization to heat is well established and has been the subject of many investigations. Following the logical treatment of Lee (1940), acclimatization to heat involves:

a. No considerable change in rate of sweating (Robinson, Turrell, et al., 1943; Taylor, Henschel and Keys, 1943), although the evidence is not all unequivocal (Christensen, 1947). Under conditions of extreme heat and humidity (dry bulb 120° F., wet bulb 93° F., effective temperature 97.2^O F.), but with a mean radiation temperature of the room below the ambient temperature by 5° to 7° F., the rate of sweat secretion of men walking on a treadmill (equivalent to 5 met per hour) increased their rate of sweat production from 1.5 to 2.15 liters per hour on the 27th day (Horvath and Shelley, 1946). According to Robinson, Turrell, Belding and Horvath (1943), the capacity for sweating at hard work does increase. Lee (1940) notes a greater sensitivity of the sweating mechanism in acclimatized men.

b. Shift of the comfort zone from winter to summer levels. (Yaglou and Drinker, 1928).

c. Lowering of the basal metabolic rate, which has already been considered and for which the evidence is divided.

d. Adjustments in cardiovascular efficiency. This is a most important item in the mechanism of acclimatization (Taylor, Henschel and Keys, 1943; Machle, 1944).

e. Adjustments in rectal and skin temperature. Not important generally, but nevertheless demonstrable (Horvath and Shelley, 1946).

f. Diminished loss of sodium chloride in sweat and urine (Morton, 1944; Johnson, Pitts and Consolazio, 1944; Lehmann and Szakall, 1937a), particularly in the former. This is an important phase of acclimatization to heat, operating to defer the onset of heat cramps.

The initial phases of acclimatization to heat, involving particularly the cardiovascular and vasomotor adjustments, are completed in a few days to a week and are expedited by work. However, Mills (1944a) claims that metabolic acclimatization, associated with changes in nutrient requirements in a tropical environment, proceeds at a much slower rate, beginning late in the second week of continuous exposure and being largely accomplished by the end of the third week. Heat acclimatization persists for at least 3 weeks of cold weather, but the benefits decrease from week to week (Henschel, Taylor and Keys, 1943).

9. UPPER LIMITS OF TOLERABLE TEMPERATURE. The upper limits of temperature and humidity tolerated by men at rest and at work have been estimated, among others, by Yaglou (1945), Bean, Eichna and Ashe (1945) and Eichna, Ashe, Bean and Shelley (1945). The estimates vary as human subjects vary, but there is general agreement that the wet bulb temperature is the limiting factor which determines the ability of men to work in a hot environment (90° F. and above). At a dry bulb temperature of 120° F., men can perform moderate work easily at a wet bulb temperature of 90° F.; they would work with difficulty at a wet bulb temperature of 92° F., and would find it impossible to continue work at a wet bulb temperature of 94° F. (Eichna, Ashe, Bean and Shelley, 1945). Acclimatized men working above the upper tolerable environmental limits develop, according to Eichna et al., "marked physiological changes, and undesirable, frequently disabling symptoms similar to those sustained by unacclimatized men when first working in the heat."

The upper temperature tolerance limit for man can be considerably raised by partial immersion of the body, or periodic immersion, in relatively cool water. Spealman (1945b) observed that nude men with their lower extremities immersed in water at 86° F. can tolerate an effective air temperature of 107° F. (127° F. dry bulb, 105° F. wet bulb) as well as men without such expedients tolerate an effective temperature of 92° F. The alleviating action of water at 86° F. sprayed on the body at high air temperatures is also demonstrated.

The increasing difficulties of men working under intolerable conditions of impaired heat dissipation are described by Gerking and Robinson (1946), Ladell, Waterlow and Hudson (1944), and Talbott (1944b), while Heilbrunn and associates (1946) discuss the more general

topics of heat death, heat injury and toxic factor. Readers interested in this phase of the subject should consult the publications cited.

10. HEAT INJURY. Lee (1940) classifies the main syndromes of heat injury as follows: (1) hyperpyrexia, or true heat stroke; (2) circulatory insufficiency, or heat exhaustion, characterized by lowered blood pressure; (3) hypochloremia, or heat cramps, characterized by a serum chloride concentration of 365 mg. per 100 ml. or less; and (4) super-dehydration, characterized by reduced salivation, oliguria, uremia and pyrexia.

The debilitating effects of dehydration are well assessed by Adolph and Brown (1943) as follows: "The survival of men in the desert without water depends upon (1) endurance (the maximum water deficit tolerable), and (2) the rate of water loss. Most men in the desert for a week can tolerate a water deficit of 5 percent of body weight without losing their capacities to participate in organized physical activity, but are less efficient than when fully hydrated. Between 5 percent and 10 percent dehydration, the average man is quite fatigued and spiritless. If much physical exertion is attempted, dehydration exhaustion occurs. After 10 percent loss of body weight as water, most men can do little more than a slow walk without a pack. For an inactive person, a tolerable water deficit of 20 percent can be predicted."

One interested in an extensive study of man's response to desert conditions can turn to Adolph's (1947) recently published book with profit.

Brown and Towbin (1944) discuss the circulatory stress of heat, work and dehydration in desert troops.

McCance (1935-36, 1937, 1938) and McCance and Widdowson (1937) have reported extensively on the metabolic and physiological effects of salt deficiency in man (see also Lévy-Solal and Laudat, 1935). An interesting relationship between chloride and nitrogen economy has been reported by Conn and Johnston (1945). From long term experiments on human subjects in a tropical environment, they observed that "a period of negative nitrogen balance is a characteristic phenomenon associated with the process of acclimatization to humid heat. This occurs invariably and is independent of the level of dietary protein and salt. It is observed at the time that the concentration of salt in urine and sweat are falling. It disappears when the adjustment called acclimatization has been completed. It is our belief that an acute physiological load imposed upon the adrenal cortices (by the stress of the new adjustments in electrolyte metabolism made necessary by life in humid heat) is responsible for both findings (decrease in urine and sweat salt concentrations and negative nitrogen balances)...After full acclimatization has been established, and salt and nitrogen equilibrium are being maintained, a sharp drop in salt intake leads to negative nitrogen balance. Under these circumstances, the addition of salt to the diet results in a rapid return to nitrogen equilibrium. From a practical point of view, such negative nitrogen balance is quickly abolished in fully acclimatized man, when the daily total NaCl intake is raised to 7 grams or above."

Conn and Conn (1941) had previously shown that adrenal cortical extract increases sodium retention and increases the excretion of nitrogen in the urine. According to Ladell (1945), desoxycorticosterone diminishes the output of sodium and chlorine in the sweat as well as in the urine.

An informative table of the physiological responses of acclimatized men to increasing effective temperatures, when at rest and at work, may be found in the 1947 Guide of the American Society of Heating and Ventilating Engineers, page 208. The table gives the responses of pulse rate and rectal temperature, the perspiration per hour, and total work accomplished.

The Composition Of Human Sweat And The Rate Of The Dermal Loss Of Nutrients.

The composition of human sweat is subject to so much variation that average values for its constituents may be as meaningless as average values for the composition of human urine. It varies with the region of the body wherein the sweat is secreted, with the rate and duration of sweating and the stage of acclimatization. It has not been shown to be affected by atmospheric conditions, and its relationship to the food supply is so variable as to defy generalization. As Adolph (1923) says: "While the composition of the sweat is correlated slightly with that of the blood, the product elaborated by the sweat glands seems to be primarily independent of chemical conditions in the body....This secretion is more dilute than the blood in respect to most

dissolved substances. The compensating activities of the kidneys which correlates their work with that of the sweat glands, is a correlation only on the part of the kidneys, since the kidneys are accustomed to correct the variations in the blood's composition.''

The dissolved substances of sweat possess no known relationship to the function of this secretion in maintaining the heat balance of the body. They seem to include all of the constituents that are found in the blood, including all the water-soluble minerals and vitamins, and organic metabolites, such as urea, ammonia, uric acid, creatinine, creatine (sporadically), lactic acid, and citric acid. The occurrence of lactic acid in sweat is particularly interesting, since its concentration in sweat far exceeds that in urine, blood, saliva and cerebrospinal fluid (Horstmann, 1941), suggesting that it bears some intimate relationship to sweat-gland activity (Fishberg and Bierman, 1932a, b). Muscular activity will increase the concentration of lactic acid in sweat, especially if the activity is so severe that a ''steady state'' is not attained (Snapper and Grünbaum, 1929). Ingested alcohol readily passes over into the sweat in which its concentration may exceed that in blood (Nyman and Palmlöv, 1936). For general information on sweat composition, the following references may be consulted: Hancock, Whitehouse and Haldane (1929), Chatron (1933), Mosher (1933), Whitehouse (1931, 1935), Hopf (1935), and List (1948).

The excretion of organic metabolites in sweat is merely an incident in the general function of ridding the body of substances of no further use to it. Presumably the greater the excretion of urea, for example, in the sweat, the smaller its excretion in the urine. If the protein metabolism of the body on a constant intake of protein is increased by the conditions, environmental or intrinsic, that have induced sweating, then the output of total nitrogen in both urine and sweat will increase. In particular, one would expect an increase in the total output of creatinine by both pathways. Information in the latter category is not available, so that in themselves variations in the output of nitrogenous constituents in the sweat afford no basis for concluding the existence of corresponding variations in protein requirements.

For the purposes of this report, the content in sweat of mineral and organic nutrients only will be considered. It is true that information of this type is not easily interpreted in terms of increased requirements until it has been shown that compensatory changes in urinary output do not occur, or do not completely compensate. The hourly output in the sweat of a given nutrient is far more significant in this connection, than the concentration in some particular sample of sweat, because (1) the composition of sweat varies in different regions of the body, (2) the method of collection may not avoid the possibility of evaporation, and (3) the frequent use of rubber devices for collecting sweat from a limited area of the body, a hand or an arm, may release from the rubber substances simulating in some of their reactions, the nutrient that is desired to be determined, i.e., ascorbic acid. The best method of collection (Lee, 1940) is to remove the sweat solutes during a definite period of time by thorough washing of the entire body. The total weight of sweat can be estimated with small error from the net loss in body weight during the collection period. This method was followed in all of the work carried out in the Division of Animal Nutrition of the University of Illinois, the results of which will be summarized below (Mitchell, Hamilton, Shields and Haines, 1943.)

1. NITROGEN AND AMINO ACIDS. As indicated above, the output of total nitrogen in the sweat may be of significance to the question of the relation of nutrition to a tropical environment. Its concentration in sweat has been variously reported from 47 to 130 mg. per cent (Talbert, Silvers and Johnson, 1927; Voit, 1933), and the total output per day from 71 mg. to 5.28 gms. (Benedict, 1906), depending upon ambient temperature and especially upon muscular activity. At a temperature of 90° F. in New Orleans, Bost and Borgstrom (1926-27) observed an output of 75 mg. of nitrogen in the sweat per hour, accounting for some 70 per cent of the difference in output of urinary nitrogen between summer and winter conditions previously observed. Bischoff, Maxwell and Hill (1931) have also reported an inverse relationship between output of sweat nitrogen and of urinary nitrogen. Talbert, Silvers and Johnson (1927) noted no relation between the nitrogen in sweat and in urine, and Berry (1915) observed no relation between nitrogen of diet and of sweat. However, Cuthbertson and associates (1934) established a clear direct relationship between the daily excretion of sweat nitrogen and the protein contents of the diet, which was varied from 70 to 180 gms. daily. At a room temperature of 15° to 20° C., the output of nitrogen in the sweat ranged from 0.118 to

0.301 gm. per m^2 per day. In the Illinois experiments (Mitchell et al.,1943), the nitrogen content of sweat averaged about 20 mg. percent., independent of environmental differences imposed, the hourly output varying from 16 mg. under comfortable conditions to 167 mg. under hot humid conditions. Regardless of their significance to the problem immediately under discussion, this information of the dermal losses of nitrogen in the sweat is of great importance to nitrogen metabolism studies carried out under conditions such that thermal or emotional sweat is produced. Metabolism experiments undertaken under sweating conditions may be seriously vitiated with reference to those elements and nutrients present in sweat in appreciable quantities, unless dermal losses are measured and utilized in the computation of body balances.

The loss of amino acids in the sweat is of immediate interest to the problem of the effect of a tropical climate on nutrition, since these nitrogenous compounds are not metabolites but unchanged products of protein digestion. Haugen and Talbert (1928), using the colorimetric method of Folin, report values varying from 1.6 to 4.8 mg. of amino acid nitrogen per 100 ml. of sweat in 73 experiments upon 23 subjects. McSwiney (1934) found an average of 5.0 mg. of amino acid nitrogen per 100 ml. of sweat for 10 women and an average of 6.6 mg. for 14 males. These values agree well with the figure of 44 mg. of the ten essential amino acids per 100 ml. of sweat reported by Hier, Cornbleet and Bergeim (1946), if one may assume an average nitrogen content of about 16 percent in the amino acid mixture of sweat. The latter investigators analyzed "normal" sweat for the 10 essential amino acids individually by microbiological methods. In these experiments the sweat was collected from the entire body except the head by incasing the nude subjects, after a shower bath, in a rubber bag as far as their necks and sweating them in a cabinet for 20 to 30 minutes, during which time 100 to 200 ml. of sweat were obtained. The following comments on the results secured are interesting:

"Our results show that the amino acids secreted in the sweat are independent of the effect of diet or food ingestion since no difference in composition is found in sweat taken from subjects in a fasting state or after eating. Furthermore, the level of the amino acids in sweat is independent of the variations in the blood. Ingestion of large amounts of amino acids, which causes a marked rise in the blood level, is without effect on the sweat amino acids. This must mean that the amino acids do not appear in the sweat merely by filtration from the blood. This is further shown by the fact that arginine and histidine are markedly higher and threonine and tyrosine are slightly higher in sweat than in plasma, while the other amino acids studied are present in approximately the same order of magnitude in both fluids. The high arginine content of sweat is particularly interesting in view of the findings of Talbert et al. (1927) that the urea nitrogen of sweat is about 4 or 5 times that of blood. Arginine may be involved in the formation of this urea by the sweat gland."

Concerning the practical significance of their observations, Hier and associates offer the following comments: "The amount of amino acids lost in the sweat is not strikingly significant in the economy of amino acids by the body. In our subjects the sweat contained about 0.44 mg. per ml. of the ten amino acids studied. Under average conditions of temperature and humidity, the amount of sweat is about 500 ml. per day. This would represent a loss of about 220 mg. per day of the ten amino acids. Even with excessive sweating in warm weather with active work when 3 liters of sweat may be formed, only 1.3 gm. of these amino acids would be lost."

It should be noted, however, that the ten essential amino acids constitute only 50 to 60 per cent of the proteins in common foods (Block and Mitchell, 1946), and that the loss of non-essential amino acids is just as much a nutritive setback as the loss of essential amino acids. Thus, 3 liters of sweat, on the basis of the findings of Hier et al., would contain 2.2 to 2.6 gms of amino acids, and 10 liters, representing an attainable daily sweat volume, would contain 7.3 to 8.6 gms.

2. VITAMINS. The water-soluble vitamins, in so far as they have been tested for in human sweat, have been found to be present in detectable amounts. The great disparity existing among published values of quantitative occurrence is probably traceable to different analytical methods and to different methods of sweat collection. The following tabulation affords a summary of published information:

Vitamin	Concentration in sweat: mcg. per 100 ml.	Reference
Thiamine	8 to 9	Hardt and Still (1941)
"	.3 to .6	Tennent and Silber (1943)
"	0 to 0.1	Slater (1942)
"	0.2 or less	Mickelson and Keys (1943)
"	.2 to .3	Mitchell et al. (1943)
"	15	Cornbleet et al. (1943)
"	0	Sargent et al. (1944)
Riboflavin	.9 to 2.4	Tennent and Silber (1943)
"	12	Cornbleet et al.(1943)
"	.7 to 1	Mitchell et al. (1943)
"	0.5 or less	Mickelson and Keys (1943)
"	0	Sargent et al. (1944)
(Nicotinic acid	20	Cornbleet et al. (1943)
(plus metabolites	100	Mickelson and Keys (1943)
"	4 to 5	Mitchell et al. (1943)
"	8 to 14	Johnson et al. (1945b)
Pantothenic acid	11.to 12	Tennent and Silber (1943)
"	30	Cornbleet et al. (1943)
"	4	Spector et al. (1945)
Ascorbic acid	500 to 1100	Bernstein (1937)
"	550 to 640 *	Cornbleet et al. (1936)
"	100 to 200	Zselyonka et al. (1937)
"	24 to 57	Wright and MacLenathem (1939)
"	0	Tennent and Silber (1943)
"	50	Mickelson and Keys (1943)
"	0	Sargent et al. (1944)
"	0 to 15	Kirch et al. (1943)
"	19	Shields et al. (1945)
Dehydroascorbic acid	20	Sargent et al. (1944)
"	60 to 150	Kirch et al. (1943)
"	70	Shields et al. (1945)
Pyridoxine + metabolites	7	Johnson et al. (1945d)
Choline	3 to 15	Johnson et al. ·(1945a)
Inositol	21	Johnson et al. (1945)
Para-aminobenzoic acid	0.24	Johnson et al. (1945)
Folic acid	0.26	Johnson et al. (1945c)

* Too high, because sweat was collected in rubber (see Kirch et al. 1943).

Selecting from this tabulation the analyses that seem to be the most reliable, judged on the basis of methods of assay and sweat collection and agreement with other results, it may be concluded that the following vitamins will generally be found in sweat in a concentration of 20 micrograms or less per 100 ml.: thiamine, riboflavin, nicotinic acid (total), pantothenic acid, pyridoxine (total), choline, inositol, p-aminobenzoic acid, and pteroylglutamic acid (folic acid). Although the human requirements for all of these vitamins are not known, the concentrations in sweat are so small as to seem insignificant in practical nutrition. The concentration of ascorbic acid in sweat is extremely variable and its presence in detectable amounts seems to be sporadic. The occurrence of dehydroascorbic acid in sweat, while quite variable in quantity, may be significant in a practical sense.

In the experience of most investigators, the concentration of vitamins in sweat is not appreciably, if at all, affected by the dietary intake, with the exception of that of dehydro-ascorbic acid (Kirch et al., 1943), pantothenic acid (Tennent and Silber, 1943) and possibly pyridoxine (Johnson, Hamilton and Mitchell, 1945d). The enormous increases in the thiamine concentration of sweat on dosage, reported by Hardt and Still (1941), have not been confirmed by others.

The hourly excretions of vitamins in the sweat observed by the Illinois group (Johnson, Spector and their associates), even under conditions inducing sweat secretion of 700 ml. per hour or more, were quite inconsiderable compared with known or probable requirements. Even the dermal loss of dehydroascorbic acid under these conditions would not exceed about 3 mg. per day.

3. MINERALS. There is a dermal loss of minerals from the body prior to the onset of sweating, mainly of sodium, potassium, chloride and sulfate sulfur (Freyberg and Grant, 1937). This loss is incidental to the diffusion of water from the subdermal tissues, the insensible perspiration. On the initiation of sweating, the insensible loss of water and minerals presumably stops where the surface of the skin is covered with a film of water.

The sensible sweat that supersedes this insensible water (and solute) loss apparently contains all of the minerals found in the blood. Besides sodium, potassium, calcium, magnesium, chlorine, sulfur and phosphorus, copper, manganese, iron (Mitchell, Hamilton, Shields and Haines, 1943), iodine (Spector et al. 1945, and earlier workers) and fluorine (McClure et al. 1945) have been identified, and concentrations and, in some cases, losses per hour, determined. The presence of considerable amounts of bromine in sweat was observed, but not measured, by Spector in the routine of his determinations of iodine in sweat. In this discussion we are mainly concerned with those minerals whose losses are of such magnitude as to possess some nutritional significance.

The copper and manganese are present in sweat in mere traces, 5 to 6 micrograms per 100 ml.

According to Bischoff, Maxwell and Hill (1931), phosphorus does not occur in thermal sweat. Talbert, Stinchfield and Staff (1933) report variable phosphorus contents in sweat ranging from 0 to 4.8 mg. per 100 ml. Mitchell et al. (1943) observed an average of 0.022 mg. percent of phosphorus in 20 samples of sweat, with individual concentrations ranging from 0.003 to 0.042 mg. percent; Whitehouse (1931) found only doubtful traces of sulphate in sweat.

The magnesium content of sweat is extremely variable (Hopf, 1935) and bears no reasonably constant relation to calcium content, although on an average, in the experience of Carpenter and Talbert (1932). the ratio is 4 of calcium to 1 to magnesium, the latter concentrations averaging 1.2 mg. percent. Hopf's average for magnesium in sweat is almost three times this figure, namely, 3.32 mg. percent.

Sweat is generally much more dilute in calcium than blood plasma, though the amounts present may be appreciable from the nutritional point of view. Subject to the usual considerable variation, the following concentrations of calcium have been reported: 0.3 to 1.5 mg. percent (Marchionini and Ottenstein, 1931), 5 to 10 mg. percent (Bryant and Talbert, 1931), 5.8 mg. percent (Borchardt, 1931), 5 mg. percent (Carpenter and Talbert, 1932; Talbert, Haugen, Carpenter and Bryant, 1933), 4.6 mg. percent (Hopf, 1935), and 1 to 3 mg. percent (Mitchell, Hamilton, Shields and Haines, 1943). The concentration seems to decrease as sweating proceeds, and values averaging as high as 12.2 mg. of calcium per 100 ml. of sweat have been reported by Hopf (1935) for initial collection. Mitchell et al. (1945) found hourly losses of calcium in the sweat over eight-hour periods averaging 5.3 mg. under comfortable conditions, and 13.0 mg. under hot humid conditions with sweat losses of 700 to 800 gms. per hour.

The potassium in sweat will generally average 45 to 50 mg. percent (Talbert, Haugen et al., 1933; Borchardt, 1931; Hopf, 1935), though much higher concentrations have been reported for initial sweat specimens. Whitehouse (1935) assesses the usual ratio of potassium, as chloride, to sodium chloride in sweat as 1 to 9.

The most important mineral component of sweat is sodium chloride and many reports of its quantitative occurrence in sweat, generally measured as chloride concentration, have appeared in the literature, extending back into the last century. There is little point in citing, or in averaging, all reported values. Lee (1940) says: "The concentrations given by different workers of chloride in heat sweat vary very much. In general, they appear to err on the high side, owing probably to evaporation occurring from the sample. Later work has indicated that the sweat seldom, if ever, becomes hypertonic as compared with the blood stream, and is

usually hypotonic." In view of the variable chloride content of sweat from different areas of the body, the most reliable method of making this determination is to divide the total chloride secreted over the entire body during a definite time, obtained by proper washing procedures, by the net loss in body weight. Using this method Lee obtained chloride concentrations in sweat, under varied environmental conditions, ranging from 166 mg. percent down to 49. According to Bock (1944), sweat sodium varies closely with sweat chloride.

The chloride content of sweat, as of many other of its properties, depends upon the rate of sweating, the degree of acclimatization to heat, and on inherent characteristics of the individual. Sweat becomes more dilute in chloride with adaptation to hot atmospheres, more concentrated in chloride as the rate of sweating becomes more profuse. "The susceptibility of some individuals to heat cramps no doubt depends in part on the inability of their sweat glands to reduce sodium chloride loss to a low level." (Daly and Dill, 1937). After adaptation Dill observed the salt concentration of sweat to drop to about 15 milli-equivalents of NaCl per liter in extreme dry heat (1933), and to about the same level (17 milli-equivalents per liter) in humid heat (1937). Johnson, Pitts and Consolazio (1944) have defined these and other conditions determining the salt content of sweat. It is interesting to note the claim of Johnston, Conn, Louis and Steele (1946) that the concentration of chloride in hand sweat represents that of the entire body. Keys (1943b), however, did not find this to be true under his experimental conditions.

While variations in salt intake in the direction of an increase over normal levels does not seem to affect the chloride content of sweat appreciably (Cuthbertson and Guthrie, 1934; Mitchell et al., 1943), there can be no doubt that severe restriction of salt intake will reduce the chloride content of sweat to very low levels (Conn et al. 1946). This conservation of salt by the sweat glands seems to be mediated by the same endocrine mechanism that favors salt conservation by the kidney, i.e., desoxycorticosterone, since Bock (1944) observed that the administration of potent extracts of the adrenal cortex of cattle to men fully acclimatized to heat decreased the level of sodium and chloride in the sweat. The association of negative nitrogen equilibrium with low salt intake and its correction by an increased salt intake, in acclimatized men has already been noted (Conn and Johnston, 1945), and is probably attributable to the same endocrine mechanism.

The dermal loss of iodine in man has been recognized since iodine balances were first performed by von Fellenberg in 1926. Spector, Mitchell and Hamilton (1945) studied the concentration of iodine in sweat and the hourly loss of iodine through the skin under different environmental conditions and with and without dosage of the subjects with potassium iodide. The results obtained can be briefly summarized as follows:

The concentration of iodine in sweat averaged about 1 microgram per 100 ml., increasing to 3.2 mcg. after a single dose of 2 mg. of KI. The hourly loss of iodine through the skin during 8 hour exposures to controlled environmental conditions varied from 1 to 5 mcg., and was not consistently correlated with the environmental conditions or with the rate of sweating.

No information on the iron content of sweat and the dermal loss of iron has been found in the literature. In unpublished experiments, Mitchell, Hamilton, Shields and Haines (1943) have reported evidence on this problem. Taking the proper precautions to avoid iron contamination, and using 4 young men as subjects, it was found that sweat contains about 2 mg. of iron per liter, using the washing method to secure the dermal loss of iron from the entire body, and taking the net loss in body weight as measuring the sweat loss. For individual tests, the variations were not extreme, the coefficient of variation of 8 measurements being 32 percent.

The hourly losses of iron under different environmental conditions are given in Table 1, each figure being the average of 4 experimental subjects over 5 experimental days each:

Table 1.

The Effect of Environment on the Hourly Dermal Loss of Iron

Temperature ºF.	Relative humidity pct.	Insensible loss in body weight gm. per hour	Hourly dermal loss of iron mg.
101	69	814	1.77
100	70	688	0.80
101	66	584	0.90
90	94	297	0.95
90	66	134	0.25
85	50	113	0.21
85	49	103	0.33
85	50	87	0.17

These hourly losses of iron through the skin are considerable compared to the daily tabolism of 10 or 15 mg. They throw a rather devastating light upon the "new theory of iron metabolism," well epitomized by Johnston (1943). According to this theory, the body finds it difficult to eliminate what iron is absorbed from the food, either in the feces or in the urine. The body iron is thus used over and over again, and is conserved to a very much greater extent than has been observed for any other mineral. However, the theory neglects entirely the dermal excretion of iron, which may evidently be considerable. Its evidence that excretion through the intestinal mucosa is negligible is not convincing, and its presumption that the body absorbs from the gastro-intestinal tract only as much iron as it needs is contrary to the known ability of the liver, and possibly other tissues, to store iron, while the mechanism proposed for the blocking of iron absorption in the intestinal mucosa, while ingenious, rests upon a tenuous basis (Granick, 1946).

Temperature Of Food And Drink.

The temperature at which food and beverages are consumed might be expected to influence the digestive processes. Eberhard (1940) has reported that ice water and ice cream retard the emptying time of the stomach by 30 to 60 minutes, while hot coffee has no effect. Cold drinks, such as may be consumed as refreshments in the tropics, also affect heart action as revealed by inverted T waves, and the author suggests a possible correlation of this effect with so-called "acute-indigestion." Gershon-Cohen and co-workers (1940) observed that cold meals seem to speed up gastric evacuation, while depressing gastric secretion during the initial stages of digestion. "Summer diarrhea might be due partly to ice-cold drinks which effect too rapid gastric evacuation of gastric contents not effectively prepared for the intestines because of the depression in gastric secretions." The reason for the apparent discrepancy between the results of these two studies needs eluciation.

Solar Radiation And Air Motion.

In the construction of weather chambers for environmental studies on man, two components of weather, wind and solar radiation, are most difficult to duplicate as they occur outdoors. variable winds of variable intensity are characteristic of outdoor life and are difficult to duplicate indoors throughout natural ranges. The spectral qualities of sunlight have never been exactly duplicated artificially. The effect of air motion and of solar radiation on the heat economy of men under tropical conditions will not be considered in any detail here; the subject is introduced merely to complete the discussion of the physiological effects of a tropical climate.

Winslow, Gagge and Herrington (1939) have found that the cooling effect of air movement varies with the square root of the velocity. Significant wind effects on evaporation from the skin through dry fabrics is found only at permeabilities above 30, greater than that of some important Army fabrics (Fourt and Harris, 1944). "Until permeability rises far above 30, fabric thickness is probably the dominant influence on physiologic efficiency in cooling." Gold (1935) has compiled a table of sensations associated with different wind velocities under different dry and wet bulb temperatures that should correlate with Houghten and Yaglou's effective temperature nomogram.

The thermal qualities of solar radiation have been referred to above. An analysis of this heat load has been presented by Blum (1945b) and seems to be equivalent to 4 kg. cals. per min., 2 or 3 times the resting metabolism of an average man. One important function of clothing in a tropic environment is to cause the reflection from the body of much, or most, of this heat load. Oppel and Hardy (1937) showed that, of the rays impinging on the skin, the more penetrating they are the less sensitive is the subject to them, and that dermal pigment plays only a small role in the thermal exchange between environment and man. However, in this section of the report, we will be mainly concerned with the actinic effects of the solar rays, producing biochemical changes in the body and biochemical damage. In this connection, reference should be made to the excellent review of Blum (1945a) on the physiological effects of sunlight on man. The physiological activity of cosmic rays and of cosmic radiocarbon (Grosse and Libby, 1947) may later be shown to be of importance, especially at high altitudes.

Sunburn is a lesion induced by exposure to intense sunlight. Its military aspects have been well presented by Blum (1943), from whom the following citation is taken: "There is evidence that dietary factors may affect the sensitivity to sunburn, but to date this has not received adequate investigation." The possible non-nutritional protective measures against sunburn have been evaluated by Blum, Eicher and Terus (1946). The presence of sweat on the skin is of importance in this connection, since a sweat film of 1 mm. thickness transmits only about 27 per cent of solar radiation effective in preventing sunburn according to a report by Crew and Whittle (1938). On the supposition that pellagra may be a result of tryptophan (or protein) deficiency, based on some experiments by Chick and Hume (1920) on monkeys, Dawbarn (1924) attempted to induce light-sensitivity in mice by placing them upon a tryptophan-deficient diet, but without success.

The consumption by farm animals of certain plants, such as buckwheat and plants belonging to the genus Hypericum may cause an abnormal sensitivity to light. The excessive consumption of chlorophyll-containing plants may induce a photo-sensitivity by the production of phylloerythrin in the digestive tract (see Blum, 1941). The dermatitis of pellagra in man is exacerbated by sunlight and by heat (Smith and Ruffin, 1937), while there is some suggestion that nicotinamide, the absence of which from the diet is reponsible for many of the lesions of pellagra, possesses a light-protective-action as yet unexplained (Kühnau, 1939).

Ultraviolet radiation of wave lengths that produce sunburn will cause injury to the eye: the cornea and conjunctiva (photophthalmia), the retina (scotoma), and possibly the lens (cataract) (Blum, 1945a). According to Jolliffe (1943) from experiments on humans, "light, within the degree used in these studies, is without great significance in the production of corneal vascularity." In the rat, intense light from incandescent lamps does not modify appreciably the riboflavin content of the retina (Bessey and Lowry, 1944), nor modify the eye changes induced by riboflavin deficiency (Lowry and Bessey, 1945). Light exposure in the human does not seem to modify appreciably the carotene requirement (Booher and Callison, 1939), though vitamin A is intimately involved in the mechanics of rod vision.

The Effect of Heat on Nutrient Requirements: Animal Experiments.

1. VITAMINS. Mills has performed many experiments on growing rats to determine the relative vitamin requirements in a cool room (65-68° F.) and in a hot room (91° F., 60 per-cent relative humidity). The procedure was quite similar in all experiments. A series of diets is prepared that is presumably adequate in all respects except for the vitamin under study, which is incorporated in the diets in graded doses. The diets are then fed ad libitum to groups of 4 to 6 rats, both in the cool room and in the hot room. The requirement in each environment is taken to be the smallest concentration of the vitamin that has induced the best growth, or that has averted symptoms of avitaminosis. With this technic Mills has concluded that the requirements for thiamine (1941), choline (1942) and vitamin K (Mills et al., 1944) are sharply increased in a tropical, as compared with a temperate, environment, but that the requirements for riboflavin, pyridoxine, pantothenic acid, p-aminobenzoic acid and inositol are not affected by the environment (1943a). The indicated increased requirements for thiamine, but not for choline, in a tropical environment, and the failure to demonstrate differences in requirements for the other B vitamins were later confirmed on chicks (Mills et al., 1947). The heightened thiamine and choline requirements in tropical heat were also confirmed for rats (1943b), having particular regard to the possible destruction of thiamine in diets kept in a hot room.

The consistency with which Mills has been able to repeat his thiamine findings is impressive, but the interpretation of his data is none the less difficult. Wide differences occurred in the intake of food in the two environments, greater amounts being consumed in the cold, while within either room, the gains in body weight secured generally paralleled the food intake. The ad libitum feeding technic, when used to assess nutrient requirements, tacitly implies that the experimental animals will consume food in proportion to its nutritive adequacy. This proposition has never been proved. With reference to thiamine in particular, Waterman and Ammerman showed with rats (1935a) and with pigeons (1935b), that increasing doses of the vitamin will stimulate growth, probably merely by stimulating food consumption, far beyond doses that would represent requirements: 160 mcg. per day for rats and pigeons was still inadequate for maximum growth, though far in excess of any reasonable estimate of the thiamine requirement. Interpretation of the Mills' experiments is difficult also because the data have not been subjected to an adequate statistical treatment, particularly incidence ratios of deficiency symptoms. The possibility has not been considered in the interpretation of incidence ratios that a tropical environment may merely visualize latent symptoms of deficiency, as light and heat serve to visualize dermal malnutrition in pellagrins.

It is difficult to conceive why the requirements for vitamins per unit of food consumed should be modified by environmental temperature, especially as markedly as Mills' evidence indicates for thiamine, since the function of thiamine in the body, in so far as it is known, relates to the metabolism of food. Possibly a tropical environment will raise the body temperature of the rat, speed up the metabolic reactions including those involving the destruction of thiamine, and thus raise the thiamine requirement per unit of food to be metabolized. Attempts to confirm Mills' results on rats in other laboratories have not been entirely successful, though the experimental procedures used have not always been above criticism.

Sarett and Perlzweig (1943) approached the problem by studying the metabolism of the B vitamins in growing rats maintained at 75° F. or 91° F. Growth, urinary excretion (except for thiamine) and tissue storage, in the two environments, of thiamine, riboflavin, pantothenic acid and nicotinic acid were measured on two diets, one containing slightly above minimum requirements of the vitamins and the other containing excessive concentrations. The food intakes of the groups at the lower temperature were restricted to those of the corresponding groups at 91° F., which were fed ad libitum. This procedure penalized the rats kept at 75° F. because of their greater caloric requirements. The urinary excretion of riboflavin, pantothenic acid and nicotinic acid averaged somewhat higher on both levels of vitamins in the hot environment, but the statistical significance of the differences between pair mates was not evaluated. At the end of 22 to 25 days, the content of the several vitamins was determined in liver and in carcass. At the higher level of vitamin supply, the retention averaged greater for all vitamins, except for nicotinic acid storage in the liver, in the hot environment, but at the lower level of vitamin supply, the reverse was generally true. The results cannot be readily interpreted in terms of requirements in the two environments, mainly because the obvious interpretations of the results on the two levels of vitamin supply are contradictory. Williams, Eppright, Cunningham and Mills (1944), using ad libitum feeding, were not able to detect differences in vitamin storages in rats at low and high room temperatures on diets containing adequate concentrations of the B vitamins, but higher dietary concentrations of thiamine and choline were offered to some of the rats in the tropical environment.

Robinson (1943) studied the thiamine requirements of growing rats at different environmental temperatures by growth and food utilization studies and by the output of pyruvate in the urine. The paired-feeding method was used throughout, but only for rats in the same environment and undergoing the same test on graded doses of thiamine. In determining the thiamine requirement at different temperatures the most sensitive method was that involving determination of the minimum amount of thiamine required to prevent an increased excretion of pyruvate in the urine. Robinson's results demonstrated a higher thiamine requirement at the higher temperatures, ranging from 0.7 mcg. per gm. of food at 15° C. to between 2.0 and 2.4 mcg. per gm. of food at 35° C.

Failure to appreciate the fact that thiamine requirements, and probably the requirements of some other B vitamins, are related to the amount of food metabolized, and therefore the food intake of the experimental animal, has introduced confusion into this problem. Kline, Friedman and Nelson (1945), administering thiamine supplements in constant amounts and allowing food ad libitum, concluded that thiamine requirement in the rat is decreased with in-

crease in environmental temperature and that this decrease is related to a decrease in caloric requirement. The thiamine-food ratio was always more favorable for the high-temperature rats, so that at the low levels of thiamine supply, they survived longer after a curative dose, or grew better, than the low-temperature rats. This experiment confirms what Amantea (1933) proved many years ago, i.e., that there is a relationship between the caloric intake of animals and the vitamin B_1 requirement.

The experiments of Edison, Silber and Tennent (1945) are subject to the same limitation of interpretation as those of Kline et al. in so far as they administered thiamine dosages in constant amount irrespective of the caloric intake. Most of the experiments reported were carried out with diets containing 20 mcg. or more of thiamine per rat per day. On such rations there was no significant difference in the concentration of thiamine in the liver, whether feeding was ad libitum or equalized, or between tropical and temperate rats. The conclusion: "Thiamine requirements for the growth of rats in a tropical environment (90° F. and 70 percent relative humidity) are not greater and may be less than in temperate conditions (72° F. and 50 percent relative humidity)," must rest upon those experiments carried out at lower levels of thiamine intake. When the intake was reduced to 2 mcg. daily or less, the weight-loss gradient was said to be much more gradual in the tropics than in temperate conditions, although the weight curves do not support this conclusion solidly. In any case, differences in activity and metabolic rates in the two climates complicate the interpretation of weight curves. The greater incidence of polyneuritis among rats in the temperate environment fed ad libitum clearly was due to their smaller thiamine-to-calorie ratio. The data cannot be considered to support the conclusion above stated.

Ferrero (1940) has reported that massive doses of nicotinamide (200 mg.) given to rabbits before heat treatment increase their resistance to heat and raises the tolerable temperature. Such doses possess no nutritional significance.

Kurokawa (1941a and b) has reported that avitaminosis A can be induced more speedily in rats in a hot environment than in a cool one, and that, with rabbits, higher temperatures can be tolerated after massive doses of vitamin A. The reviewers have not had access to these reports.

The distressing variation exhibited by different rats in assays for vitamin D has led investigators to study all possible factors, with reference to the selection of test animals and to the environment that might be brought under better control. From a statistical study of their experiences with this assay Tourtellotte and Bacon (1935) suggested that room temperature may be a factor, since their results indicated, though not very strongly, that rats are more sensitive to rickets at room temperatures of 80° F. or above. Two years later, Guerrant, Dutcher and Crowthers (1937) subjected this suggestion to systematic study. Comparable experiments were performed at 73°, 84°, and 100° F., using a uniform rachitogenic diet and carefully selected test animals. The severity of rickets was measured by x-ray examination of the bones, the line test, the ash content of the bones, and the calcium and inorganic phosphorus in the blood serum. The mass of data obtained led the authors to believe "that environmental temperature is not an important consideration in either the production or the cure of rickets in the rat."

However, variable food intakes--lesser food consumption in the hotter rooms--complicate the interpretation of the data, expecially since the authors admit: "In our regular vitamin D assays, where all animals are maintained at a comparable temperature, those animals which make the greatest increase in body weight [and presumably consume the greatest amount of food] invariably show the highest degree of rickets." This confirms the recorded experience of Watkins and Mitchell (1936). When on the rachitogenic diet, the rats in the warmer rooms, consuming less food, showed slightly severer rickets as judged by the line test, but not by the other criteria, which may have been less sensitive. It is probable, therefore, that if the rats in the warmer rooms had consumed as much food as those in the cool room, they would have exhibited a more marked difference in the severity of rickets at the end of 21 days of feeding.

The results of Guerrant et al. may, therefore, be considered to support the presumption that the sensitivity of rats to rickets, and probably their requirements of vitamin D, are enhanced in a hot environment.

There is some slight suggestion that high temperatures, in so far as they induce hyper-pyrexia, may increase the requirement for ascorbic acid, if one may so interpret decreases in the content of the vitamin in the tissues of animals subjected to artificial fever (Martini and Torda, 1937; Zook and Sharpless, 1938). Haas (1939) from experiments on rats, guinea pigs and rabbits, concluded that ascorbic acid curbs the increase in body temperature induced by drugs and by high external temperatures.

2. PROTEIN. Mills (1944b) having previously shown to his own satisfaction that sub-sistence in a tropical climate raises sharply the required concentration in the diet of thiamine and choline felt some concern about the matter of protein requirements. This concern arose from the fact that foods high in the B-vitamins are generally high in protein, and that high-protein foods are often eschewed in hot weather and climates because of their high heating effect, commonly referred to as their specific dynamic action. Hence, he carried out an ex-periment on growing rats, using the technic already described, to determine the protein re-quirements for growth in cool and hot environments. The protein used was casein, without and then with a cystine supplement, and the dietary levels tested ranged from 6 to 36 percent, with 4 rats to a diet group.

The average data reported are quite irregular for the rats in the cold room. They are interpreted by Mills to mean that, for unsupplemented casein, the growing rat requires a greater concentration in the diet in the hot than in the cold environment, but for the supple-mented casein, no difference in requirement exists. This anomalous conclusion needs much better evidential support than Mills' experimental data afford before any credence need be given to it. The protein requirement of growing animals is not directly related to the amount of food to be metabolized, as are, in all probability, the B-vitamin requirements; rather it is related to the gain in weight and the size of rat. When Mills' data for the first 3 weeks of feeding are analyzed, it will be found that the relationship between gain in weight and protein intake follows the same curve in both hot and cold rooms.

The Effect of Heat on Nutrient Requirements: Experiments on Human Subjects.

1. ENERGY. A tropical environment seems to have no consistent effect upon the basal requirement of energy (Mason, 1940), and where effects have been noted they are not consid-erable, being of the order of 10 to 15 percent, and generally in the nature of a depression of the rate characteristic of a temperate climate. Muscular activity is reduced, especially the severer forms. On the other hand, the lighter weight clothing worn in the tropics permits the performance of many types of activity with a smaller expenditure of energy per unit of work (Gray, Consolazio and Kark, 1947). Appetite may be adversely affected in the tropics, at least until acclimatization is attained, and the consumption of adequate calories may be dependent more than usual upon the appetite appeal and tastiness of the food offered. The importance of an adequate caloric intake for troops in the field under conditions of severe work in a tropical environment has been emphasized in many writings by qualified observers, among which the report of Brown and McCreary (1943) may be cited here. In another report, Taylor (1946) says, speaking of diet and fluids: "Hot weather presents no peculiar problems other than taste, custom and supply. Palatability is essential to combat the prevalent ano-rexia as assurance for good nutrition."

Van Veen (1942) calls attention to the low fat consumption in Java, 5 to 12 gms. per day per adult of 50 kgm. consuming 2600 calories, even in the most prosperous section of the population. He is of the opinion that one should not speak about a "requirement-norm" for fat, but only of a "habit-norm." The danger of a deficiency of linoleic acid is minimized, should such a requirement be established for man, since the fats from rice and maize, coconut and peanut, probably contain a sufficiency of unsaturated fatty acids found to be essential for the rat.

2. WATER AND SALT. The requirements for water and salt are markedly affected by a tropical environment and are so interdependent that they must be considered together. The greater the output of water in the sweat the greater the requirements for both water and salt, while the greater the intake of salt the greater the requirement of water.

It is obvious that the loss of water during sweating will increase the water requirement

by a like amount minus the compensatory decrease in urinary water, with any correction, one way or the other, dependent upon changes in the evaporation of water from the respiratory passages. These latter factors are probably relatively inconsiderable under conditions inducing severe sweating. The experience of trained observers of men working in a tropical environment, both in the laboratory and in the field, emphasizes the importance of replacing these water losses continuously.

Pitts, Johnson and Consolazio (1944) express their well-founded conclusion as follows: "The best performance of fully acclimatized young men on a good daily diet, performing intermittent hard work in the heat, is achieved by replacing hour by hour the water lost in sweat. Any amount of water considerably less than this leads in a matter of hours to serious inefficiency and eventually to exhaustion."

The need for water may actually outstrip the thirst for water. "It should be emphasized that during work men never voluntarily drink as much water as they sweat, even though this is advantageous for maintaining heat balance, but usually drink at a rate approximating about two-thirds of the water loss in sweat. Although cool water is more palatable, water at any temperature up to 100° F. is equally beneficial. The deficit is made up in the rest periods following the day's work" (Pitts et al., 1944).

The experience of the Armored Medical Research Laboratory at Fort Knox, Kentucky, is described by Nelson and Bean (1942) in the following words: "...for the mild desert conditions (maximum temperature around 110° F.) limitation of water to 4 quarts a day resulted within a period of days in operational inefficiency." And further "...water consumption was substantially the same whether water was taken only at meal times or taken when thirsty. Those who delayed drinking until meal time experienced considerable discomfort without any apparent advantage in water economy or physical well-being. Drinking in small amounts when thirsty would seem to be the ideal practice..."

The additional amount of water required in a tropical over a temperate environment will vary widely with environmental conditions, with muscular activity and from man to man. In a report to the Food and Nutrition Board of the National Research Council, Hastings and Guest (1944) state that while 4 liters of water per day may suffice for men at light work at a maximum temperature of 95° F., for men at heavy work at a temperature of 113° F., the requirement may be raised to 13 liters.

The need for extra water during work in the tropics is much more urgent than the need for extra salt. Replacement of salt losses hour by hour, unlike the replacement of water, has no demonstrable advantage (Pitts et al., 1944). The salt loss can be replaced just as well at meal time. Taylor and co-workers at the University of Minnesota (1943) studied the effects of 3 levels of salt intake on the cardiovascular functions of 49 unacclimatized men at work and at rest during exposure to hot dry conditions, water being allowed ad libitum. The salt was administered with the meals, and the exposure periods were of short duration, i.e., 2 to 3.5 days each. With day temperatures of 120° F. dry bulb and 85° F. wet bulb, and night temperatures of 85° to 95° F. dry bulb and 65° to 75° F. wet bulb, daily intakes of 4 to 8 gms. of salt were found to be inadequate, being associated with higher pulse rates and rectal temperatures, poorer postural cardiovascular adjustment, greater loss in body weight, and a salt deficit of 13 gms. in 3 days. On the other hand, a high intake of salt, 28 to 32 gms. daily, showed no advantages over a moderate intake of 13 to 17 gms. daily, even though the sweat produced amounted to 5 to 8 liters daily. These experiments, it should be remembered, were carried out on unacclimatized men in observational periods of only 2 to 8 days.

According to Conn and Johnston (1944), there exists in fully acclimatized men an adaptive mechanism "whereby salt concentration of the sweat is remarkably and consistently diminished when the need for salt conservation becomes acute." Their experiments involved balance studies on acclimatized men over periods of 50 to 80 days performing hard work (4100 to 4600 cals. per day) in a tropical environment (85° F. and 85 percent relative humidity), and producing 5 to 9 liters of sweat daily. Under these conditions it was possible to maintain salt equilibrium on a total salt intake of 6 gms. daily. One subject was able to establish equilibrium on less than 3 gms. of salt daily. In conclusion the authors of this interesting report state: "We believe that these studies indicate that salt supplements are not needed and may actually be deleterious; that the average diet containing 10-15 gms. of NaCl

affords adequate protection against salt depletion."

Certainly there seems to be a wide margin between the usual intake of salt and the day's requirements under moderate environmental conditions. These requirements have been assessed at 5 gms. daily by Hastings and Guest (1944) and 2 gms. daily or less by Falconer and Lyall (1937).

If, and when, it becomes necessary to supply salt in forms other than food, the use of salt tablets may be resorted to. Consolazio, Pecora and Tusing (1947) have devised a slow-dissolving non-irritating salt tablet for use in hot environments. However, the trend in modern research and thinking is against the need, or advisability, of administering salt to men working in the heat either in tablet form or as salinized drinking water, except possibly in the case of unacclimatized men. The modern view is well stated by Pitts, Johnson and Consolazio (1944) as follows: "It would appear from the present experiments that in the case of well-acclimatized young men, whose daily diet is adequate, the best performance of intermittent work in the heat is to be achieved by replacing water loss hour by hour and salt loss meal by meal."

3. PROTEIN. Whether the inhabitants of tropical or sub-tropical regions voluntarily select diets lower in protein than inhabitants of temperate regions seems to be a controversial question. It is difficult to dissociate diet selections based upon economic status and availability of food supplies from selections based upon physiological motivations. Perhaps as clear an expression as has been secured of physiological factors, relatively uncomplicated by economic factors, is obtained by studying the diet selections of college students in temperate and sub-tropical sections of the United States. Denis and Borgstrom (1924) studied the urinary nitrogen output of college students in New Orleans and found the indicated protein intake to be low, 74 gms. daily, and to be lower in the summer months than in the winter months. The later report by Borgstrom and Bost (1926-7) further confirmed the presumption that climatic conditions affect the voluntary intake of protein. However, Youngburg and Finch (1926) found as low an output of nitrogen in the urine in college students at Buffalo as had been observed previously in New Orleans, with no observable tendency for the urinary nitrogen to decrease during the summer months. Apparently, the question whether climatic factors per se modify the protein appetite of man cannot be answered except on the basis of more extensive statistical surveys.

Caspari and Schilling (1920) followed the nitrogen metabolism of 2 individuals at rest and at work in Berlin, and during periods spent on the west coast of Africa. The diets consumed in both localities were quite similar, containing about 1.1 gms. of nitrogen and 33 cals. per kgm. body weight per day. The subjects were generally in negative nitrogen balance in all tests, apparently due to an inadequate caloric intake, but the balances in the tropical regions (determined with due regard to dermal losses) are not distinguishable from those in the temperate regions. Also, the intestinal utilization of nitrogen, fat and energy was not significantly different in the two climates. The authors conclude that the body uses food in the tropics as efficiently as elsewhere, and, in particular, that nitrogen balance can be maintained as easily in Africa as under similar dietary conditions in Berlin.

In unpublished experiments, Mitchell, Hamilton and Haines studied the nitrogen metabolism of 4 men under comfortable and under hot-humid conditions, on different levels of dietary nitrogen, approximately 13, 15 to 16, and 21 to 23 gms. daily. The collection periods were 5 days in length, on each of which the subjects were confined to the experimental rooms for 8 hours. The experiments lasted from late January through May. At the lowest levels of protein intake, the sweat nitrogen amounted to less than 1 percent of the intake in the comfortable environment and to 10 to 11 percent of the intake in the hot-humid environment. The nitrogen balances for all subjects were less under the latter conditions than under the former by about 1 gm. of nitrogen daily. At the higher levels of intake, however, no consistent differences in nitrogen balance were noted in the two environments.

If a condition of pyrexia is induced by residence in a tropical environment, an increase in the endogenous catabolism of body protein, as revealed by an increased output of creatinine in the urine, is to be expected. Such an effect of elevated body temperature on creatinine output in the urine was clearly shown by Myers and Volovic (1913) in experiments on rabbits in which hyperthermia was induced artificially by infection. Both Shaffer (1908) and McClure

34

(1918) have observed the same phenomenon in acute febrile conditions in humans, together with creatinuria, indicating an accelerated endogenous catabolism of nitrogen. According to Graham and Poulton (1912) a febrile condition may or may not increase the total protein metabolism depending upon the availability of other sources of food energy.

While it is probable that a tropical climate may increase the endogenous catabolism of protein if it induces an elevation of body temperature, there are no good grounds for believing that the protein requirements of men will be appreciably altered in the tropics, particularly after acclimatization.

4. VITAMINS. The concentration of vitamins in sweat (see above) is not sufficiently great to modify appreciably the vitamin requirements of man in a sweating environment, even under extreme conditions of sweating, with the possible exception of ascorbic acid. However, the observations of Fox (1940), to be cited at more length below, do not reveal any grounds for believing that the ascorbic acid requirements of man are increased under extreme sweating.

Some suggestions have appeared in the literature that a warm environment modifies the vitamin requirements of man. Holt (1943) has observed a greater urinary excretion of thiamine in hot weather and the reverse in cool weather. He interprets this parallelism between environmental temperature and urinary thiamine output as an indication of a lessened requirement for the vitamin in a hot climate and hence a greater spill-over in the urine. However, this parallelism may not be so easily interpretable. In the Division of Animal Nutrition of the University of Illinois, in similar experiments on pigs in a controlled environment, the relative thiamine output in the urine in a hot as compared with a cold environment may be different on a high as compared with a low thiamine intake. On a low intake we checked the observation of Holt on man, but on a high intake, the urinary thiamine was very much less in the hot than in the cold (unpublished experiments). The ratio of thiamine to dietary calories was kept the same in both environments. A decreased excretion of thiamine in the urine in a hot as compared with a cool environment was also reported for rabbits by Iwamoto (1941).

Williams, Mason, Wilder and Smith (1940) in their studies of the thiamine requirements of psychopathic patients believed that they observed a climatological factor. A diet restricted to 0.15 mg. of thiamine was tolerated by 4 subjects for 147 days during the summer months before deficiency symptoms developed. A similar diet given to 4 other subjects in the winter months could be tolerated for only 88 days. Since symptoms of thiamine deficiency developed earlier in the winter months, there is a suggestion that the requirement is greater in the winter than in the summer. However, there is no assurance in these experiments that the body stores of thiamine were the same in the subjects observed in the summer months as in the subjects observed in the winter months; that body stores of thiamine were an important determinant in the outcome of the experiments is indicated by the long deferment of deficiency symptoms on a grossly inadequate intake.

An elevated body temperature, such as may be induced by work in the tropics, has been observed to lower the blood plasma concentration of ascorbic acid in man by Daum, Boyd and Paul (1939) and to decrease the urinary output (see also Zook and Sharpless, 1938); Hausberger and Nevenschwander-Lemmer (1939) observed a more rapid disappearance from the blood of injected ascorbic acid in patients with fever than in normal persons; Zook and Sharpless (1938) and Falke (1939) have presented evidence of much the same significance, though Craig et al. (1946) were not able to demonstrate an effect of fever on the level of ascorbic acid in the blood of patients in whom fever was induced by physical means or by the use of chemotherapeutic agents.

However indicative such observations of the effect of fever on ascorbic acid requirements of man may be, the reviewers have found no direct evidence that the requirements are raised in the tropics even under conditions of severe work. The negative evidence obtained by Fox (1940), experimenting with large groups of native laborers in a Witwatersrand Gold Mine in South Africa, is especially significant. Having concluded from a critical review of the literature that "A net daily intake of 15 mg. appears to be all that is required, not only to protect the average individual from scurvy, but also to maintain him in good health," Fox (1940) carried out an extensive study on two groups of 950 mine laborers, each during a

period of 7 months. "The groups were chosen so as to be as comparable as possible in respect of tribe, age, physical condition and occupation. One group remained on the usual mine diet, which was estimated to contain 12 to 25 mgm. ascorbic acid, while in the other, an additional daily ration of 40 mgm. vitamin C was administered in the form of orange juice concentrate." The low order of the reserves of ascorbic acid in these native miners is revealed by low plasma values (less than 0.3 mg. percent and generally less than 0.2 mg. percent) and by the results of a saturation test. Twelve cases of scurvy occurred in the control group during the course of the experiment and one mild case in the supplemented group.

"Otherwise, no significant difference could be detected between the two groups. Thus the change in weight was almost identical and there was no evidence forthcoming that the general health, physical efficiency, condition of the gums or resistance to infection had been improved." The examination of the gums of the experimental subjects was carried out by a dental surgeon and the physical efficiency tests by persons trained in physical education. The latter tests, aimed at measuring the main components of physical efficiency, namely strength, skill and endurance, were consistently negative.

Although the temperature and humidity of these Witwatersrand gold mines are not, strange to say, given in Fox's article, from other articles (Dreosti, 1935-6; Cluver, 1932) it is evident that the temperatures and humidities are severe, about 95° F. and close to saturation. The experiments of Fox may, therefore, be interpreted to mean that the ascorbic acid requirement of men working in hot-humid surroundings is not elevated appreciably, and is in fact of a surprisingly low order of magnitude.

5. MINERALS. The only evidence relating to a possible effect of a hot environment on the mineral (other than common salt) requirements of man, of which the reviewers are aware, was secured in unpublished experiments by Mitchell, Hamilton and Haines at the University of Illinois. Such an effect would be expected largely on the basis of mineral losses in the sweat, which have been discussed above. In these experiments it was shown that the iodine, calcium and iron losses in the sweat were of such magnitude as to modify requirements appreciably provided compensatory conservation of these elements by other excretory channels did not occur.

With reference to iodine, balance experiments on 4 subjects showed that conservation of iodine by the kidneys compensated for dermal losses so that the iodine balance was not less in a hot humid than in a comfortable environment (see Spector et al., 1945, for most of these data).

For calcium, both at a low daily intake of about 715 mg. and at a high intake of about 1670 mg., compensatory factors did not operate effectively, and the calcium balance in the hot-humid environment was less than that in the comfortable environment by 100 mg. daily at the low level of intake and by over 400 mg. at the high level. These statements relate to average balances for 3 or 4 men. The individual balances were somewhat irregular and the obvious interpretation may not be statistically significant, though strongly suggestive. An increased fecal output of calcium, more than an increased dermal output, determined the generally less favorable balance of calcium in the tropical environment.

In the same series of studies, iron balances were obtained on three subjects during 2 weeks under comfortable conditions and 2 weeks under hot-humid conditions. With iron intakes somewhat higher in the latter environment because of a greater consumption of tap water, the dermal loss of iron averaged 2 mg. per 8 hours under comfortable conditions and 10 mg. per 8 hours under hot-humid conditions. The iron balances in 5 of 6 possible comparisons, favored the temperate environment, the average difference amounting to over 6 mg. per day. The results are highly suggestive of an increased iron requirement in a tropical climate due to sweat losses of iron, but the data are inadequate to establish the point with a satisfactory degree of certainty, the probability of a chance outcome being 0.040. In these experiments the intake of iron was abnormally high, 50-60 mg. daily.

The Effect Of Diet On Tolerance To Heat And Humidity: Experiments And Observations on Human Subjects. The evidence bearing on the possibility of increasing man's tolerance to a tropical environment by dietary modifications is conflicting. Foulger (1942) has reported tests on men working in extreme heat and high humidity indicating a marked increase in the

resistance to heat cramps and heat prostration following the ingestion of vitamin C tablets. These tests have not been reported, in so far as the reviewers are aware, in sufficient detail to permit critical appraisal.

The experiments of Fox (1940) on native workers in the Witwatersrand gold mines of South Africa, referred to above, revealed no benefits to men working in intense heat brought about by ascorbic acid supplementation of a diet of borderline content.

Because of claims, widely quoted in the popular press, of special benefits of ascorbic acid for men working at high temperatures, workers at the Laboratory of Physiological Hygiene at the University of Minnesota (Henschel et al.,1944) undertook an extensive experiment to test such claims under controlled experimental conditions. Forty-four normal young men were subjected to temperatures up to 122° F., and low humidity, for periods of 3 hours to 4 days. Work on a treadmill, equivalent in calorie expenditure to 7 times the basal metabolism, was imposed daily in 6 ten-minute work periods alternating with rest periods of 10 minutes. The basal diet was restricted in vitamin C content to 20 to 40 mg. daily in one series of experiments, and to foods, in the other series, of low content of the vitamin. A supplement of 500 mg. of ascorbic acid was given daily to half of the subjects, the other half receiving placebos.

Many observations were made on the test and control subjects during the exposure periods. Pulse rates in rest and in work, rectal temperatures, vasomotor stability tests (Crampton's blood ptosis test), rates of sweating, general observations and subjective reports "all failed to demonstrate any significant advantage for the men receiving supplements of ascorbic acid...Psychomotor tests and strength tests likewise generally failed to show any advantage in the ascorbic acid supplementation. There apparently was a slight gain in flicker fusion frequency related to the extra intake of vitamin C." This test is commonly used as an index of fatigue of the retino-cortical system. Daily sweat losses ranged from 5 to 8 liters and contained only inappreciable quantities of vitamin C. "Heat exhaustion occurred with equal frequency in the vitamin C restricted and the supplemented groups."

The same group of workers (Henschel, Taylor, Mickelsen, Brozek and Keys, 1944) have reported in abstract the results of experiments similar to the above but designed to test the effect on heat tolerance of combined dosages of thiamine, riboflavin and nicotinamide. High intakes of these vitamins had no appreciable beneficial effect on the physiological, biochemical or psychomotor functions measured. "The rate and degree of acclimatization, the incidence of heat exhaustion and the ability to do hard work in the heat were not influenced by the vitamin supplementation contrary to the claims of others." Some details of these experiments are contained in a report to the National Research Council by Henschel, Taylor and others (1943).

In the course of their experiments on work in the heat as affected by intake of water, salt and glucose, Pitts, Johnson and Consolazio (1944) state, with no amplification: "We have been unable to detect any advantage from administering 200 mgm. of ascorbic acid, 20 mgm. of thiamine hydrochloride, 20 mgm. of riboflavin or large doses of brewer's yeast, either singly or together either during work or the day before."

Experiments possessing a different significance were reported by Droese in 1942 from the Kaiser Wilhelm Institute in Berlin. Fourteen subjects were instructed to pedal on a bicycle ergometer to complete exhaustion, indicated objectively by high pulse frequency and by hypoglycemia, under two environmental conditions and with or without certain supplements added to their ordinary freely-chosen diet, presumably, since no description of the basal diet is given. The rooms were maintained at 20° C. and 57 percent relative humidity, and at 39° C. and 30 percent relative humidity. The dietary supplements consisted of 50 gm. of glucose or 50 gm. of glucose + 500 mcg. of vitamin B_1 (Betaxin). The supplements were given in cocoa, while during control periods the subjects received cocoa with saccharine added to simulate the sugar supplement.

Unfortunately only average results are given with no statistical analysis of the data. When the supplements were given in the work period when the subjects felt tired, the outcome seemed clear cut: The endurance of the subjects was increased in the cool room by glucose alone or by glucose plus the vitamin, the increases averaging 14 and 24 percent, respectively.

In the warm room, however, the glucose alone was without effect, while the glucose plus betaxin increased endurance an average of 23 percent. The work capacity in the warm room was less than half that in the cool room, but the muscular efficiency, expressed in calories produced per kgm. m. of work, as well as the rate of sweating, was the same in both rooms. When the supplements were administered one-half hour before the work periods, some experiments were inconclusive.

The author concludes that the vitamin B_1 requirement is increased by work in the heat, not because of increased sweating nor of a diminished efficiency of muscular work, but probably because of some circulatory impairment preventing the rapid removal from the muscle of intermediary products of sugar metabolism that accumulate there in the absence of adequate concentrations of vitamin B_1. As indicative of circulatory impairment in the heat there was a slight lowering of pulse frequency after glucose plus B_1 as compared with glucose alone. However, this lowering of pulse frequency occurred in both the cool and the hot environments.

The experiments of Droese were carefully planned and executed. The outcome would be clearer if supported by statistical analysis. With no knowledge of the thiamine content of the basal diet, it is impossible to decide whether the added 0.5 mg. is satisfying an increased requirement in the hot, no symptoms of thiamine deficiency having been·observed; whether it is alleviating a non-nutritional condition, such as the favorable effect of niacin in alleviating hepatic damage in the aged (Rafsky and Newman, 1943); or whether it is increasing tolerance to heat as dietary carbohydrates increase tolerance to cold (Keeton et al., 1946).

Pitts, Consolazio and Johnson (1944) have failed to detect any effect of the amount of dietary protein on physical fitness in hot climates. Van Veen (1942) has called attention to the very small content of fat in the diets of some tropical populations, but without any implication that low fat intakes favor tolerance to heat. No investigation seems to have been made of the possible effect on heat tolerance of modifying the proportions of fat and carbohydrates in the diet, similar to the work of Keeton et al. (1946) and of Mitchell et al. (1946) with reference to cold tolerance.

Conclusions. From animal experimentation, it may be concluded that in a hot environment the requirement for thiamine is definitely and rather markedly increased. There are indications that ascorbic acid requirements may also be increased if the body temperature is raised, and that the sensitivity of animals to rickets may be enhanced in a hot environment. However, the methods of maintaining heat balance in most of the lower animals and in man are so different that animal experimentation may be an insecure guide to human needs and reactions in this area of science.

Direct experimentation on human subjects, supplemented by observations in the field, show:

1. That energy requirements are decreased in a hot climate, as compared to a temperate climate due to a diminished basal expediture of energy, or to greater efficiency in certain types of muscular work, associated with lighter clothing, or to a lessened capacity for work and less motivation or to all three. The effect of tropical heat on the basal metabolism is not a consistent one and evidence on this item in the above statement is conflicting.

2. The water requirements are definitely increased when sweating is induced and somewhat in proportion to the amount of sweat secreted. The daily requirement of water may increase from 2.5 to 3.0 liters per day in a temperate climate to 13 liters or more during work in a hot environment. For the maintenance of physical fitness under the latter conditions it is imperative that water losses in the sweat be covered by water ingestion at short intervals. During intense sweating, thirst is not an adequate guide to water requirements, though if thirst is satisfied continuously any considerable dehydration may be avoided for the usual working periods.

3. The salt (NaCl) requirements of man may be greatly increased from a level of 2 to 5 gms. daily under non-stress conditions to 15 to 17 gms. daily under conditions of profuse sweating, 8 to 10 liters daily. This large increase is confined to the period of acclimatization and the salt losses in the sweat need not be replaced continuously, as in the case of water

losses. In fact, replacement at meal times by the consumption of food seasoned with salt in the usual fashion may be adequate. When acclimatization to heat supervenes, salt conservation in sweat and urine greatly lowers the dietary salt needs, which may be but little raised above requirements in a temperate climate. In any case, the need for salt tablets, or salinized water during muscular work under tropical conditions, so greatly emphasized 5 or 10 years ago, seems now to be restricted to unusual situations prior to the attainment of acclimatization.

4. There is no adequate statistical evidence that men voluntarily select low-protein diets in a hot climate, regardless of food availability and economic status. Observations in the field indicate no benefits in body heat economy from the consumption of low-protein diets. Laboratory experiments show that protein requirements may be increased slightly by (a) a stimulation of tissue catabolism if pyrexia occurs, and (b) by sweat losses of nitrogen uncompensated by diminished losses in the urine. Considering all evidence it may be concluded that protein requirements may be slightly increased in the tropics by some 5 to 10 gms. daily.

5. The great preponderance of evidence from human experimentation shows that, despite small losses of vitamins in the sweat, vitamin requirements are not appreciably increased over the values in a temperate climate by residence or by work in a tropical climate.

6. Due to losses of minerals in the sweat, and, in the case of calcium, to fairly consistent increases in fecal losses in a hot environment, man's requirement for iron, and less certainly for calcium, may be increased in a tropical environment. The problem deserves further study.

7. Attempts to increase man's tolerance to heat, or to accelerate acclimatization to heat, by dietary modifications have not been as extensive as the importance of the problem warrants. No evidence has been secured to suggest with any assurance that modification of the proportions of protein, carbohydrate and fat in the diet will improve heat tolerance, but little work has been undertaken with well-controlled procedures in this direction. Most of the evidence on vitamins--most of it secured with ascorbic acid--has not revealed any benefits from supplementary doses to diets presumably adequate in vitamins under temperate conditions. The case with reference to thiamine and exhausting work in the heat, especially when extra calories are furnished by sugar, needs further study, in view of the evidence of Droese of a favorable effect of the vitamin on the capacity for doing work in the heat.

Conclusions concerning the relationship between nutrition and "tropical deterioration," based largely upon extensive observations of allied troops during the late war, have been expressed by Kark and co-workers (1947). The following quotation is noteworthy: "In providing rations for soldiers at least three considerations are of prime importance. First, a considerable variety of food items should be issued. Second, the food items should be much the same as soldiers are accustomed to in ordinary life, but emphasis should be placed on acceptable foods of high biological value. Third, caloric deficits must be avoided. From the standpoint of military efficiency, caloric deficiency was an important problem during the war; vitamin deficiencies relatively unimportant."

The proper packaging and storing of foods is emphasized also in these and other reports of a similar nature, since the preservation of perishable nutritional factors--mainly the vitamins--in the diet under the unfavorable conditions of the tropics is as important as the proper selection of foods.

Reference may also be made to the article by Johnson (1943) on nutritional standards for men in tropical climates. In discussing this subject, the main thesis of this section of the report, one must guard against sweeping conclusions based upon negative evidence. As Van Veen (1942) has pointed out, there is much less certain knowledge on human nutritional requirements in the tropics than on requirements elsewhere.

IV. DIET AT ALTITUDE

THE PHYSIOLOGICAL EFFECTS OF ALTITUDE. The physiological effects of altitude are occasioned by diminished atmospheric pressure, diminished partial pressure of oxygen, increased intensity of solar radiation and changes in the proportion of radiations of different wave lengths in the sun's rays. These effects are experienced at high elevations on the earth's surface, but particularly in high-altitude flying.

1. CHANGES IN SOLAR RADIATION. Speaking of the solar spectrum as affected by altitude, Laurens (1938) states: "On entering the earth's atmosphere 5 percent of the total radiation (1.93 g. cal. per sq. cm. per min.) is ultra-violet, 52 percent visible, and 43 per cent infra-red. Owing to extinction and absorption by the time the radiation reaches the earth's surface the relative amounts have changed and at average heights of the sun with a total radiation intensity of 1.0 g. cal. per sq. cm. the distribution is ultra-violet 1 percent, visible 40 percent and infra-red 59 percent. Total intensity is primarily dependent upon height above sea level, as well as upon seasonal and daily variations, which particularly influence the ultra-violet. Abbot shows that only 75 percent of the total solar radiation (the solar constant) reaches a level of 1800 meters, and only 50 percent to sea level. Spring sunlight is the strongest and richest in infra-red, the autumn sun by comparison being richer in ultra-violet, the maximum content of which is reached in the summer." See also Blum (1945b).

The ultra-violet rays are responsible for the nutritional value of sunlight with reference to the functions of vitamin D in the body. They are also responsible, on intense application, for tissue injury, such as sunburn, and injury to the cornea, retina and possibly the lens of the eye. But the visible and infra-red rays, being more penetrating, exert deep tissue effects. The therapeutic effects of long-waved luminous and short-waved infra-red rays are well known (Laurens, 1936). The effects of visible radiations of different wave lengths on the albino rat have been studied by Allardyce et al. (1942), and of visible and infra-red radiation by Luce-Clausen and Brown (1939a, b). Pigment, either natural or artificial, does not appear to protect the deeper regions of the skin from excessive heating due to infra-red irradiation (Foster, 1935). Smith and Ruffin (1937) believe that the heating effects of the sun's rays (infra-red), rather than the visible rays themselves, are responsible for the exacerbation of dermatitis in pellagrins exposed to sunlight.

Kestner (1921) has presented some observations secured upon dogs indicating that sunlight, not reduced partial pressure of oxygen, is the effective agent in increasing the hemoglobin content of the blood at altitude. These experiments on the effect of sunlight upon blood regeneration, receive support from the observations of Foster (1931) on the effect of irradiation with a quartz mercury arc of rats receiving a milk diet. While irradiation did not alter the initial decline in blood hemoglobin, after the fourth week on the anemia-producing diet when the hemoglobin had reached its lowest level, the irradiated, in contrast to the controls, showed a marked recovery. However, the outstanding effect of ultra-violet irradiation on blood regeneration relates to the red cell count, rather than to hemoglobin concentration, in nutritional anemia (Andes and Beard, 1934) in rats and in hemorrhagic anemia (Laurens and Mayerson, 1931) in dogs. In experimental hemolytic anemia (Mayerson and Laurens, 1931) in dogs, the beneficial effect of radiant energy is exerted upon both red cell number and hemoglobin concentration. In previous work (1928), Mayerson and Laurens showed that repeated irradiation of normal animals with the flaming carbon arc stimulates the hematopoietic system to a sustained production of a greater than usual number of red cells. The latter finding was not confirmed by Sinclair (1933) on pigs, nor does the pig, made anemic by milk feeding, respond in increased red cell count and hemoglobin formation to the daily application of radiant energy from a mercury vapor lamp over a period of 38 days.

2. EFFECTS OF DIMINISHED ATMOSPHERIC PRESSURE. The literature concerned with the physiology of high altitude has not been reviewed as adequately as the importance of the subject would warrant. The earlier literature is reviewed by Schneider (1921) and later contributions are discussed in a small book by Gemmill (1943). Gemmill has also published

a later review (1946) covering reports printed during 1944 and 1945. The article by Ivy (1946) on high altitude problems in aviation may be consulted to advantage, also. Books on aviation medicine contain physiological information too, and among such books the following may be cited: Armstrong (1943), Jokl (1942) and Ruff and Strughold (1942).

a. RESPIRATORY HEAT AND WATER LOSS. This review will consider only a few selected topics in the general field of the physiology of altitude. The effect of altitude on the respiratory metabolism is of direct interest to the subject of this report. Matthews (1932-3) has concerned himself with the heat loss from the body through the lungs and respiratory passages, in vaporizing water, releasing CO_2 from solution and warming the inspired air. At ground level in dry cold air, 15 to 25 percent of the total heat production is lost in this way, while at high altitudes a much greater proportion is so lost, due to the rapid respiration required to obtain the needed oxygen. The computations show that "unless the inspired and expired air differ in oxygen tension by about 5 mm., even if clothing is so perfect that it prevents any heat loss from the skin, the body temperature cannot be maintained. By extrapolation from figures for alveolar air up to 23,000 ft. ...it appears that these conditions will be realized somewhere round about 30,000 ft." Marshall (1946) considers the respiratory water loss at ground level and at altitude and finds it to be only slightly higher per liter of exhaled air at 30,000 ft. than at sea level.

b. BASAL METABOLISM. Although the basal metabolism of man or of animals is commonly, and rightly, considered as among those physiological measurements most accurately made and most constant from day to day, the demonstration of the effects of changing environmental conditions on metabolism when these effects are small is a difficult technical problem. This is true because the possible effect is a measurement of a difference between two much larger quantities, one the measurements sans the effect and the other the measurement with the effect. Hence, the experimental evidence for such effects is so often confusing and equivocal. This situation is illustrated by the previous discussions on the effect of heat and of cold on metabolic rate. With reference to altitude, the problem is further complicated by technical difficulties inherent in low-pressure physiology such as the "blowing-off" of carbon dioxide due to an altered type of respiration, and the respiratory removal of gaseous nitrogen from the tissues. The first phenomenon disturbs the metabolic significance of the respiratory quotient of the subject and of the output of carbon dioxide; the latter phenomenon would contra-indicate the use of a closed circuit spirometer type of instrument, such as the Benedict-Roth, because of the accumulation in it of expired excess nitrogen. These phenomena, of course, are temporary, terminating after a period of adjustment of variable length.

Lewis, Iliff and Duval (1943) have discussed critically the evidence reported in this country on basal metabolism at different altitudes on the earth's surface, and have concluded, in harmony with their own observations, that altitudes varying from sea level to 7148 ft. are without appreciable effect on the basal metabolic rate of men and women. Where an effect has been presumed, the indications point to an increased metabolism at altitude. Herxheimer, Kost and Ryjaczek (1933) refer to European work up to that date and report observations of their own on 4 subjects upon whom many basal metabolism measurements were made at Berlin and at Jungfraujoch at an altitude of 11,384 ft. The Douglas-bag method was used in these studies. No consistent differences in oxygen consumption under basal conditions were noted at the two localities.

For higher altitudes, simulated in decompression chambers, the evidence is not readily reconciled. Clinton, Thorn and Davenport (1946) observed a decrease in basal metabolism (at ground level) of subjects exposed to 12,000 ft. for 3 hours daily over a 4 week period. However, the decrease was slight (4 or 5 percent) and was probably in the authors' judgment a result of an inadequate caloric intake evidenced by a slow decline in body weight. Also, in unpublished experiments by Eckman et al. from the Aviation Research Laboratory of Columbia University (1945), and by Nims and Olmstead (1945), no change in the basal oxygen consumption at altitude was noted. In earlier work, Christensen (1937) noted a linear relationship between work intensity in human subjects and oxygen uptake, undisturbed by altitudes up to 5340 m., from which it may be concluded that, at the no-work level, the oxygen uptake is also undisturbed within this altitude range. However, Cook (1945) found that a decrease in total pressure, with no reduction in the partial pressure of oxygen, inhibited the growth of chick embryos, interfered seriously with the metamorphosis of the meal worm, lowered the heat production of anesthetized and unanesthetized mice, and depressed the resting (not basal)

metabolism of 8 human subjects in proportion to the diminution in total pressure. The depression in human metabolism amounted to 24 percent at 38,000 ft. In the latter experiments, the time after the meal is not indicated and the temperature is not always given. The author concludes that:

"The evidence derived from isolated cells and from several groups of mammals appears to support the thesis that reduction of total gas pressure, quite independent of oxygen tension, alters the normal oxidation metabolism. Concerning the biophysics of the process, little if anything can be said at present."

Since the results of Cook were criticized because the subjects were not under basal conditions and because of possible technical errors, Berg and Cook (1946) carried out later experiments on the carbon dioxide production of men, both under basal and non-basal conditions, at sea level and at a pressure equivalent to an altitude of 30,000 ft. It is to be noted that the tests at altitude were started a few minutes after the desired altitude was attained, and in all tests the subjects breathed pure oxygen. With 9 subjects there was an average depression in the basal carbon dioxide production at altitude of 6.4 percent, exhibited by all but two of the subjects. The average depression was significant at the 1 percent level. Under non-basal conditions the depression in CO_2 production averaged somewhat higher and was highly significant. In these experiments no attempt was made to determine whether the depression in metabolism is caused by reduced total pressure or reduced partial pressure of oxygen. The results would be of more significance for the purposes of this report if some assurance could be felt that the tests were not carried out during a period of adjustment to the lowered pressure.

c. AEROEMBOLISM. Aeroembolism, or decompression sickness, is a result of diminished total atmospheric pressure and is now known to be caused by the liberation of gases, mainly nitrogen, from solution in the tissues of the body. In a strict sense, aeroembolism should refer to the formation of gas bubbles within the circulatory system, but the term has been extended to cover bubble formation in any of the tissues. The symptoms of aeroembolism will depend upon the location of bubble formation, whether in the joints (the "bends"), the pulmonary circulation (the "chokes"), the brain ("staggers"), or elsewhere.

There have been many recent contributions to the problem of aeroembolism, but only a few will be referred to here. The pathogenic factors and pathological consequences of decompression sickness are considered at length by Catchpole and Gersh (1947), the symptomatology by Gray and associates (1946), the relationship of aeroembolism to traumatic calcification by Allan (1945), and the incidence of decompression sickness, and its various manifestations (including syncope) by Brown (1946), Motley et al. (1945) and Smedal, Brown and Hoffman (1946), with reference to high altitude flight. Houston (1947a) has studied the occurrence of "bends," scotomata and hemianopsia at altitudes below 20,000 ft. According to the latter author: "Pilots who make repeated rapid ascents, even to moderate altitudes, may be expected to experience bends, and perhaps visual defects, even as low as 18,000 feet." Behnke (1941-2, 1945, 1947) has directed particular attention to the relationship between the incidence of "bends" and the fat and water content of the body. Obese persons are more susceptible to decompression sickness following ascent to high altitudes or from diving depths than men of normal weight, because of the greater solubility of nitrogen in fat than in water. The tolerance of various species of animals to rapid decompression parallels values for basal metabolism per kgm. of body weight, according to Behnke.

The recurrence of decompression sickness on re-ascent to high altitude (38,000 ft.) after variable periods of rest at ground level was reported by Rodbard (1947b), and the effects of cold and rate of ascent on the disease incidence by Griffin and others (1946). Hodes and Larrabee (1946) observed a close relationship between alveolar carbon dioxide tension and susceptibility to decompression sickness; though the cause of the relationship is not known, it may involve acid-base changes. Quoting from this paper: "...susceptibility increases with pCO_2 ... Subjects were forced to descend whenever the alveolar pCO_2 was more than 43 mm. Hg (seven cases). In contrast no subject was forced to descend when his alveolar pCO_2 was less than 38 mm. Hg (five cases) Between 38 and 43 mm. Hg subjects were forced to descend in 57 percent of their tests (61 cases)."

An effective method of preventing decompression sickness (aeroembolism) is the removal of dissolved nitrogen from the body prior to ascent by oxygen breathing. Using an —

aesthetized dogs, Karel and Weston (1947) showed a linear regression for both arterial and venous blood between nitrogen content and time of denitrogenation. Complete denitrogenation could not be achieved in a resting dog in less than 6 hours of continuous oxygen inhalation at atmospheric pressure. The effectiveness of denitrogenation in man has been studied by Gray, Mahady and Masland (1946) and by Henry and Cook (1945). From this work it appears that one hour of denitrogenation before ascent will protect an aviator against the severe symptoms of bends and chokes for one-half hour at 45,000 ft. Henry and Cook stress the fact that oxygen inhalation for one or two hours defers only slightly the onset of symptoms but reduces strongly the severity of the pain. Stevens et al. (1947) have measured the variation among individuals in the rate of denitrogenation, especially as these variations are determined by body weight, age, height and fat content.

Attempts to avoid decompression sickness by selection of resistant personnel on the basis of the results of repeated decompression in an altitude chamber have been reported by Gray and co-workers (1947). Quoting the authors: ''Although selection on the basis of a limited number of chamber flights of the type employed is able to distinguish groups having different mean susceptibilities, the procedure is costly in terms of personnel eliminated, and not very effective in segregating highly resistant groups.'' A possible feasible basis for selection is suggested by the high correlation between rate of nitrogen elimination through the lungs during oxygen inhalation and susceptibility to decompression sickness reported recently in abstract by Stevens, Ryder and Ferris (1947).

Particularly since the development of the pressurized cabin in airplanes, the penalty of explosive decompression has become a matter of concern. Observations of explosive decompression injuries in experimental animals have been reported recently by Edelmann et al. (1946) and by Corey (1947). Whitehorn, Lein and Edelmann (1946), in studies on dogs subjected to explosive decompression under conditions designed to minimize coincident anoxia, noted thoracic and abdominal distention in all animals, with hemorrhages in the pulmonary and gastrointestinal systems in some. With explosive decompression of sufficient severity, bradycardia and a drop in systemic blood pressure occurs. In a later paper (Whitehorn, Lein, Edelmann and Hitchcock, 1947), a rise in cerebrospinal fluid pressure was observed to result from explosive decompression of anesthetized dogs; the rise is considered to be ''a reflection of a similar rise in intrathoracic pressure.''

d. ABDOMINAL GAS. During decompression, gases present in the gastrointestinal tract, whether swallowed or formed there, will expand and under certain conditions may cause abdominal pain, at times incapacitating in its severity. Blair et al. have recently made an intensive study of this phenomenon at the Department of Physiology, University of Rochester School of Medicine and Dentistry, under a contract with the Office of Scientific Research and Development (1943). The gas content of the digestive tract for adult male subjects is about 1 liter (Blair, Dern and Bates, 1947), but is subject to great variation on account of variation in the amount of air swallowed and the amount of gas produced in the tract by fermentation. In studies of intestinal gas in simulated flight to 35,000 to 38,000 ft., Blair, Dern and Smith (1947) used 9 subjects and over 109 flights. Among the conclusions drawn from these investigations, the following may be mentioned: (a) difficulty with abdominal gas in flight is dependent not so much on the quantity as on its distribution in the tract, incapacitating pain being associated with excessive amounts in the lower part of the small bowel; (b) the only fairly consistent relation of gas discomfort to particular items of a freely chosen diet is found with carbonated water drunk prior to flight and with the consumption of melons; (c) while the ordinary variations of the proportions of protein, carbohydrate and fat in the diet seemed to be unassociated with susceptibility to abdominal gas pains in flight, extreme variations presented a different picture in that ''high-protein'' diets (19 percent of total calories as protein) with high fat content (53 percent of total calories) proved definitely superior to high-carbohydrate and normal diets in lowering the incidence of abdominal pain and its severity.

The gaseous exchange between the blood and the lumen of the gastro-intestinal tract was studied by McIver, Redfield and Benedict (1926), who developed exponential equations for predicting the absorption of oxygen and carbon dioxide under different pressure gradients. This phenomenon was recently reinvestigated by Pogrund (1947) using human subjects. Of special interest to this discussion is the demonstration by Pogrund that oxygen inhalation, by lowering the partial pressure of nitrogen in the blood, will appreciably increase the absorp-

tion of nitrogen from the intestinal tract. Hence, denitrogenation prior to flight will tend to decrease intestinal gases and the incidence of gas pains, as well as the incidence of aeroembolism.

3. SOME EFFECTS OF DIMINISHED PARTIAL PRESSURE OF OXYGEN: ANOXIC ANOXIA. The profound metabolic effects of altitude are due to the low partial pressure of oxygen in the inspired air, leading to profound changes in the respiratory process, in the oxygen transport to the tissues and in the capacity of the tissues to perform their normal functions under hypoxic conditions. Only brief reference can be made here to the large volume of literature dealing with these effects of anoxic anoxia.

a. EFFECTS ON RESPIRATION. Dripps and Comroe (1947) have reported studies of pulmonary and cardiovascular response to the inhalation of air containing low percentages of oxygen in human subjects at rest. The circulatory system (pulse rate) is readily stimulated by a reduction in oxygen percentage from 21 to 18. Respiration is stimulated only slightly at 16 percent oxygen and markedly only at 8 percent. "It is likely that the vasomotor center is stimulated more and/or depressed less by anoxia than is the respiratory center." Chambers et al. (1947) from experiments on unanesthetized dogs trained to breathe through a mask and valves, conclude "that, during anoxemia, a chemical factor, other than carbon dioxide, as well as reflex stimulation from the aortic and carotid receptors is responsible for the respiratory response." The ineffectiveness of carbon dioxide as a respiratory stimulant in anoxia has been demonstrated a number of times, most recently by Ivy, Grodins, Adler and Snapp (1947). In fact, in eleven tests on five dogs, carbon dioxide inhalation during anoxia produced respiratory depression, rather than stimulation, under conditions that could not have involved anoxic collapse. According to D'Angelo (1946 c) the modifications in the respiratory metabolism at altitude are "collectively indicative of a respiratory alkalosis."

Recent studies of alveolar air during simulated flights to high altitudes by Fenn, Rahn and Otis (1946) and by Rahn and Otis (1947), and of the oxygen pressure gradient from alveolar air to arterial blood during rest and exercise at sea level and at altitude by Lilienthal, Riley, Proemmel and Franke (1946), should be consulted for information on these topics.

One of the outstanding contributions of physiological research to military aviation is the development of an oxygen inhalation equipment for pressure breathing, first described by Gagge, Allen and Marbarger (1945). By increasing the oxygen pressure in the lungs throughout the respiratory cycle by 8 to 12 inches of water, it is possible to maintain the effectiveness of oxygen inhalation up to an altitude of 45,000 ft., or with some individuals up to 50,000 ft. Studies on the use of this equipment have been reported by Barach and associates (1946, 1947) and Eckman, Barach et al. (1947). Reports by Bateman and Sheard (1946) on the insignificant effect of pressure breathing on the cutaneous temperature of the extremities, and of Molomut and Allen (1946) on effects of cardiac output and the circulation, are worthy of consultation. Although pressure breathing may increase greatly the work of respiration (Rahn, Otis, Chadwick and Fenn, 1946), its effect on the total metabolic rate is probably slight (Bateman and Sheard, 1946). In the experience of Ivy, Atkinson, Adler, Burkhardt and Thometz (1944), pressure breathing in most cases has no effect on the total incidence of bends and chokes, although an occasional individual highly susceptible to these conditions may show marked improvement during pressure breathing.

b. SOME EFFECTS ON THE CIRCULATORY SYSTEM. In normal young men, exposures of 10 to 48 minutes to pO_2 corresponding to altitudes of 18,000 to 28,000 ft. does not induce cardiac dilatation nor affect appreciably the stroke volume or efficiency (Keys, Stapp and Violante, 1943). As the respiratory rate increases, the blood pH shifts to the alkaline side due to the washing-out of CO_2 (Clarke, Marshall and Nims, 1944). In dogs, the blood-clotting time is shortened in hypoxia, sometimes to one-half the normal value (Griffié, Chardon and Ruffieux, 1942-44), an effect that does not occur in adrenalectomized dogs. Quastel and Racker (1941) showed "that a substance, important in the kinetics of blood coagulation is produced with greater ease from tissues when these are incubated under anaerobic conditions than when incubation occurs aerobically," observations that may have a bearing on the hypoxia of high-altitude flight. Capillary permeability does not seem to be appreciably modified by anoxemia (Hopps and Lewis, 1947).

The most important effect on the blood of diminished oxygen pressure at high altitudes

relates to the oxygen saturation of the hemoglobin and the oxygen transport to the tissues. Arterial oxygen saturation, according to Houston (1946a), is extremely sensitive to even small changes in pulmonary ventilation: "Increasing the resting ventilation by half, a change of which the subject is scarcely aware, may increase arterial saturation by 10 to 20 per cent." But the predominant effect of increasing altitude is a progressive and marked decrease in hemoglobin oxygen saturation (Henson, Goldman et al.,1947) from 97 percent at sea level to about 89 percent at 10,000 ft. and to 70 percent at 20,000 ft. while breathing air. While breathing pure oxygen, these percentages are greatly increased, only dropping to 70 percent at some 45,000 ft. These percentages may fall appreciably at any altitude during a short period of moderate to heavy work (Lilienthal, Riley and Proemmel, 1946).

c. EFFECTS ON ENERGY METABOLISM. In a preceding section it was pointed out that, according to available evidence, the basal metabolism of man is not appreciably affected by moderate altitudes attainable on the earth's surface. The evidence for higher altitudes is less complete, but indicates either no effect or depressions of 6 to 8 percent, attributed not to anoxia but to low total atmospheric pressure.

The metabolism of energy is normally stimulated by the ingestion of food, the specific dynamic action, but particularly by muscular work. These stimulations call for an increased consumption of oxygen. Under anoxic conditions the supply of oxygen to the tissues is limited. An important problem, therefore, is the effect of this limitation in oxygen supply on specific dynamic action and on the metabolism of muscular work. Giaja (1938) classifies the heat-producing oxidations in homeotherms into two categories, i.e., those that are not affected by a decrease in oxygen tension, and those that are. In the former category he places the basal metabolism and the calorigenic actions of certain drugs. In the second category he places the specific dynamic action of protein. However, in a recent Russian report (Alekseev et al., 1945), which we have seen only in abstract, the specific dynamic action of a high-protein meal (broiled lean beef) was tested at an altitude of 4200 m. The increase in basal metabolism of 4 subjects was not substantial and the specific dynamic action was said to be normal. The subjects were kept warm throughout these tests and the authors surmise that previous reports of a decrease in specific dynamic action were evidently due to cold exposure.

Fuhrman, Fuhrman and Field (1945) measured the rate of oxygen uptake in vitro of the tissues of rats subjected to progressively decreasing pressures until death occurred. When compared with control tissues, the oxygen consumption of the liver and cardiac muscle of the anoxic rats was found to have decreased 20 percent and 35 percent, respectively, while that of the kidney cortex, the skeletal muscle and the cerebral cortex was essentially unchanged.

While an oxygen supply in excess of normal has been shown to have no favorable effect on the working metabolism of a man or on the recovery period (Benedict, Lee and Strieck, 1934), a deficient supply of oxygen, as at altitude, has been shown repeatedly to limit the capacity for muscular work (see, for instance, Foltz and Ivy, 1943; Christensen, 1945; Cook and Strajman, 1945) and to prolong the recovery period. The mechanical efficiency of work is not, however, impaired according to the very careful experiments of Christensen, who showed further that up to an altitude of 5340 m. the unreduced ventilation volume increases up to 120 liters per min. during muscular work, while the reduced ventilation volume per unit of oxygen uptake remains constant. Christensen believes that the pulmonary ventilation is the factor limiting work capacity at altitude, while Cook and Strajman conclude that the basic disturbance is an increase in the rate at which an oxygen debt is incurred and a retardation in the rate of recovery. At altitudes as high as 40,000 ft., however, there may be some impairment in muscular efficiency (Hall and Wilson, 1944).

Edwards (1936) observed an increase in blood lactic acid after standard work performance on first going to high altitudes, but that after acclimatization lactic acid values similar to those at sea level are found for a given performance. The following quotation suggests a reasonable interpretation of the effect of anoxia on muscular metabolism:

"The ability to perform work is lessened progressively with increase in altitude, hence also the ability to accumulate lactic acid. Only slight increases over rest values of lactic acid are found during work at 6.14 km. The inability to accumulate large amounts of lactic acid at high altitudes suggests a protective mechanism preventing an already low arterial saturation from becoming markedly lower by shift of the O_2 dissociation curve through acid

effect. It may be that the protective mechanism lies in an inadequate oxygen supply to essential muscles, e.g., the diaphragm or the heart."

According to Schneider and Clarke (1929): "Healthy unacclimatized men can do a moderate amount of physical work at a barometric pressure of 290 mm. (equivalent to an altitude of 25,000 ft.) for a short time without much distress and without harm." Karpovich and Ronkin (1946) have compared the oxygen consumption of men varying in weight from 120 to 220 pounds while working on a special ergometer simulating the cockpit of a plane. While muscular efficiency does not vary with body size, there are, of course, large differences in lung ventilation and oxygen consumption. According to Schmidt (1939), oxygen deficiency during muscular work at altitudes of 4 to 5 km. leads to complete collapse in a short time, injury to the nervous system, rather than to the muscular system, being the deciding factor.

d. EFFECTS ON CARBOHYDRATE METABOLISM. Anoxia in some degree of intensity may be expected to modify metabolic reactions, but the surprising thing is that the modifications produced are so slight. Since the efficiency of muscular work is not affected at altitude, the essential reactions involved in muscular metabolism are not disturbed, except quantitatively in limiting the capacity for doing work. Rosenthal, Shenkin and Drabkin (1945) have reported experimental findings on dogs suggesting "that a destruction of respiratory enzymes or a critical deficiency of co-enzymes in the brain is not a primary consequence of anoxia nor do such factors account for the development of irreversible functional and histological alterations that may follow anoxia."

In experiments on fasting guinea pigs, Murray and Morgan (1946) compared blood sugar levels and tissue glycogen contents at sea level and at 20,000 ft. The changes were not as striking as previously reported by others, consisting of a significant rise in blood sugar but no significant increase in liver glycogen and an actual decrease in total carcass glycogen. Wickson and Morgan (1946) observed a significant increase in blood sugar and liver glycogen in fasted rats exposed to reduced pressure, but no change in muscle glycogen. Riboflavin deficiency prevented these former effects, probably by impairing gluconeogenesis or glycogenesis or both. The previous experiments on laboratory animals revealing an initial hyperglycemia, followed by a moderate hypoglycemia were reported by Van Middlesworth, Kline and Britton (1944). Exposure of rats for 24 hours to diminished pressure induced substantial increases in liver glycogen according to Evans (1934) and Nims, Langley and Clarke (1946). According to the latter workers, maximum liver glycogen was observed at a simulated altitude of 20,000 ft., with lesser accumulations at higher and lower altitudes--a truly anomalous observation. A depletion of liver glycogen on exposure of animals to low pressures for 5 hours was also reported by Lewis et al. (1942). Thorn et al. (1942) and Reynolds (1947) found that discontinuous exposures of animals to lower pressures leads also to appreciable reduction in liver glycogen stores.

The hypoglycemic effects of insulin in rabbits are antagonized by brief periods of anoxia, with a quicker recovery of the blood sugar to normal levels, while prolonged anoxia leads to an aggravation of the hypoglycemia and a progressive fall of the blood sugar (Gellhorn and Packer, 1940). Glickman and Gellhorn (1938) observed in rats that insulin convulsions are greater in severity with a shortened latent period under low pressure.

Another type of disturbance in carbohydrate metabolism induced by anoxia has been reported by Greig and Govier (1943) in experiments on dogs. In vitro studies on the tissues of animals subjected to anemic anoxia or to anoxic anoxia revealed an extensive dephosphorylation of cocarboxylase, evidently produced by tissue anaerobiosis.

In man, the disturbances of carbohydrate metabolism by altitude are not so clear cut, possibly because the recorded observations were generally carried out at the moderate altitudes obtainable on the earth's surface. Ferraloro (1929) observed higher elevations of blood sugar after a large dose of glucose on a high mountain (2900 m.) than at a lower level (240 m.). The sugar tolerance was not modified within this range of altitude. In acclimatized subjects, the effect of altitude (up to 6140 m.) on blood sugar was less clear (Forbes, 1936). The behavior of the blood sugar in work was approximately the same at all altitudes. Baičenko and Krestovnikov (1933a) found no relation in a group of men between elevation (4200 to 5633 m.) and blood sugar level, while Kreienberg and Gerke (1942) obtained a decrease in the blood sugar in man during the inhalation of an oxygen-low gas mixture corresponding to an altitude

of 8000 m. The results are interpreted to mean a diminished sugar output by the liver in anoxia.

Leipert and Kellersmann (1942) gave a group of young men 50 gms. of glucose and then subjected them to altitudes of 5500 to 6200 m. The height of the hyperglycemic phase of the blood sugar curve was little altered by decreased pressure, but the hypoglycemic phase was shortened or completely suppressed. Phosphate metabolism was markedly affected by hypoxia; the inorganic phosphorus of the blood and of the urine was notably decreased. The decline in inorganic phosphorus in the blood was compensated by a marked increase in the content of phosphoric acid ester. According to the authors, phosphorylation, a reaction that under normal conditions is independent of oxygen supply, becomes a regulating mechanism in hypoxia making adaptation to an increased carbohydrate turnover possible.

Bryan and Ricketts (1944) obtained no evidence that the human adrenal cortex is influenced by chronic intermittent anoxia, in contrast to the results of animal experiments. Pincus and Hoagland (1943) observed an increased excretion of ketosteroids in the urine of men after test flights, correlated with flying ability.

An increased lactic acid content of the blood in men at altitude seems clearly established (Baičenko and Krestovnikov, 1933b), especially at altitudes above 18,000 ft. (Friedemann, Haugen and Kmieciak, 1945). At the higher altitudes the pyruvic acid level in the blood increased also. Both changes were prevented by breathing oxygen. The observations of Hartmann and Muralt (1934) are not so clear cut.

It is interesting to note that while alcohol absorption is increased at high altitudes, its normal slow rate of removal from the blood is similar at ground level and at altitude (Bornstein and Loewy, 1931). However, after alcohol ingestion, the R.Q. is lower at altitude, approaching that of the combustion of pure alcohol. At neither level was a specific dynamic action of alcohol observed.

e. EFFECTS ON NITROGEN METABOLISM. Certain abnormalities in the nitrogenous components of urine have been observed at altitude. In fasting pigs exposed to low percentages of oxygen in the inspired air (7 to 9 percent), Brunquist, Schneller and Loevenhart (1924) noted generally (in 6 out of 7 pigs) an increased nitrogen elimination, an unaltered proportion of urea and ammonia nitrogen, a lowered creatinine output and an increased output of creatine. There was also an increased excretion of organic acids and of acetone.

In human urine secreted at altitude, Hopf (1929) noted a greatly decreased proportion of urea nitrogen on total nitrogen (59 percent), and Loewy (1930) a percentage of 75. Sundstroem's (1919) observations of the protein metabolism of men at different altitudes are inconclusive. Residence in high mountains has been associated with an increased porphyrinuria by Lang (1939a,b) and with an increased occurrence of imidazole bodies in the urine by the same investigator in the same year.

f. ANOXIA AND ASCORBIC ACID METABOLISM. Sacerdote (1938a, b) has observed in guinea pigs and rabbits subjected to low oxygen pressures a notable increase in the ascorbic acid content of the blood and a decrease (with the guinea pigs) in the ascorbic acid content of the adrenals.

g. EFFECTS ON THE ALIMENTARY TRACT. Van Liere has been particularly active in studies of the effect of anoxia on the alimentary tract and his review article (1941) may be consulted to advantage. His book on anoxia and its effects on the body (1942) includes discussion of the alimentary tract as well as other major systems of the body. From the nature of the problem and the experimental procedures that must be used in its solution, most of the investigations of the effect of anoxia on the digestive system have involved the use of laboratory animals.

The gastric emptying time of rats fed corn oil and then exposed to a partial pressure of oxygen of 53 mm. Hg (7.03 per cent oxygen) for periods up to 4 hours was initially accelerated, but at the end of 4 hours there was no significant difference in the amount of fat remaining in the stomach between exposed and control animals (MacLachlan, 1946). In human subjects, Van Liere (1937) has observed a definite prolongation of the emptying time of the

stomach during anoxemia, the altitude threshold for persons at rest lying between 6000 and 8000 ft. On the other hand, McDonough (1943), using a group of 19 men, noted that barium sulfate passes through the stomach and progresses through the small intestine in approximately the same manner when at simulated altitudes of 38,000 ft. for two hours as at ground level. Anemic anoxia in dogs has been found to accelerate the propulsive motility of the small intestine while anoxic anemia has an antagonizing effect (Van Liere, Northup and Stickney, 1944; see also Van Liere, Northup, Stickney and Emerson, 1943). According to Malméjac and Chardon (1942-44), gradual decompression in dogs caused, first, a short period of hyperactivity of the intestine and then hypotomy at the equivalent of 5000 m. These apparently conflicting results on gastro-intestinal motility under anoxia are not readily reconciled.

Anoxia seems to depress the secretion of saliva (Filippovich, 1940) more readily than the basal secretion of the stomach (Van Liere and Vaughan, 1941), which in turn is depressed at higher pressures than the secretion of intestinal juice (Northup and Van Liere, 1939; Pickett and Van Liere, 1939). Gastric secretion provoked by food responds sooner to the depressing effects of anoxia than does the basal secretion. These facts may be interpreted to mean a decreasing oxygen requirement gradient. In man, also, low oxygen pressures depress the secretion of HCl in the stomach (Hartiala and Karvonen, 1946).

In cats and dogs, no degree of anoxemia compatible with life has any appreciable influence on the absorption of water from the stomach (Sleeth and Van Liere, 1937b), but absorption of water from the intestine is accelerated at low oxygen pressures (equivalent to 10.56 percent of oxygen and less) (Van Liere, David and Lough, 1936). Anoxia depresses the intestinal absorption of sodium chloride but not that of sodium sulfate or magnesium sulfate at pressures of oxygen compatible with life (Van Liere and Sleeth, 1936; Van Liere and Vaughan, 1940; Van Liere, Northup, Stickney and Richard, 1947). Only extreme degrees of anoxia depress the absorption of fat (MacLachlan and Thacker, 1945) or of glucose and glycine (Northup and Van Liere, 1941).

h. ANOXIA AND RENAL FUNCTION. A marked depression in urine volume at low partial pressures of oxygen has been reported for the dog by Van Liere et al. (1935-36), Malméjac (1944) and Malméjac, Chardon and Cruck (1945). In the rat, however, Silvette (1943) observed a polyuria on exposure for three-hour periods to low barometric pressures, somewhat in proportion to the pressure imposed. In anemic anoxia, induced by carbon monoxide poisoning, the urine volume decreased.

In carefully controlled experiments on human subjects exposed three times weekly for two hours to a simulated altitude of 18,000 ft., Burrill, Freeman and Ivy (1945) noted a temporary rise in the excretion of sodium, potassium and chlorine and in urine volume, followed by compensatory reduced excretions so that the totals for the twenty-four hour period were unaltered. During prolonged exposures to 8000 and 10,000 ft. simulated altitudes, no appreciable change in total urine output of men was observed by D'Angelo (1946a) under conditions of restricted food and water intake, but the renal excretion of phosphorus was significantly decreased.

A general brief discussion of anoxia and renal function has been presented by Maegraith and Havard (1946).

i. EFFECTS ON THE NERVOUS SYSTEM. The nervous system is most sensitive to anoxic anoxia. Barach (1937) calls attention to the terrible weariness and restlessness following a day's mental work at 11,500 ft., and the increased fatigability at somewhat higher altitudes and the slowness and clumsiness at all work. Brown et al. (1944) describe in some detail the nervous system dysfunctions observed during the program of high-altitude (38,000 ft.) oxygen-controlled indoctrination at Maxwell Field; the severe symptoms observed in a small proportion of the 40,000 individuals studied occurred not only during the period of great change in atmospheric pressure, but also after exposure to high altitude and even after return to ground level.

The duration of consciousness at altitudes up to 32,000 ft. after interruption of the oxygen supply was studied by Mackenzie and others (1946). At 26,000 ft., nine out of ten men were helpless within 5 minutes. "The average time to helplessness was 220 seconds. For

49

each 1000 ft. increase in altitude between 26,000 and 32,000 feet, the duration of useful consciousness decreased by approximately twenty seconds." Hoffman, Clark and Brown (1946) report the results of similar studies and correlate the duration of consciousness in anoxia at high altitudes with the associated blood oxygen saturations.

Interesting studies of the effect of anoxic anoxia on the central nervous system as revealed by the electroencephalogram have been reported on the rat by Kessler, Hailman and Gellhorn (1943) and by Engel, Webb and Ferris (1945) on man. Significant changes in the records obtained were demonstrable in human subjects at altitudes of 10,000 ft. "The degree of frequency change at 39,000 feet breathing 100 percent oxygen with the constant flow system was the same as that found at 10,000 feet breathing air...Acute alcoholic intoxication of a degree likely to be experienced by most healthy individuals drinking socially provoked electroencephalographic changes roughly equivalent to those found at 16,000 feet. Severe intoxication produced more marked changes...Reduction of blood sugar to levels of 44 to 49 mgm. percent also provoked changes in the electroencephalogram roughly equivalent to that seen at 16,000 feet."

At altitudes of 6000 m. or above, eye-hand coordination shows considerable deterioration (Muido, 1946). Functional and organic injuries to the nervous system induced by anoxia in laboratory animals have been reported by Ikemune (1940) and by Altmann and Schubothe (1942).

From experiments on human subjects, Otis, Rahn, Epstein and Fenn (1946) conclude that acapnia and anoxia are additive rather than antagonistic in their effects on contrast discrimination and steadiness. At each altitude there exists an optimum alveolar air compositing for each type of performance, optima that may differ for different types of performance. "Performance impairment in most individuals breathing naturally at air-breathing altitudes is essentially a matter of anoxia alone."

j. EFFECTS ON THE EYE. The eye has been shown to be extremely sensitive to anoxia, and the importance of good vision, especially scotopic vision, to airplane combat has furnished the stimulus for a large volume of experimental study of the eye at different partial pressures of oxygen. For general discussions of the subject, the reader is referred to an article on "Ophthalmic aspects of acute oxygen deficiency" by McFarland, Evans, and Halperin (1941), to Gellhorn and Hailman's (1943) article on "The effect of anoxia on sense organs," devoted mainly to the eye, and to Hartline's (1946) "Problems of visual physiology during the war."

Dark adaptation is definitely impaired by anoxic at partial pressures of oxygen where other sensory tests have failed to show reliable changes (McFarland and Evans, 1939). The authors state: "However, these effects are probably of no great practical significance in relation to night blindness in a pilot until altitudes of approximately 10,000 to 12,000 feet are attained." The opinion is expressed "that the changes are not concerned with the photochemical substances of the retina but with the neural elements of both the retina and the central nervous system." McDonald and Adler (1939) induced an anemic anoxia in their subjects by the inhalation of a mixture of equal volumes of nitrogen and of air. The rod and cone thresholds were raised equally in this state of anoxemia but the rate of dark adaptation was unaltered. The impairment in the visual thresholds of both rods and cones induced by vitamin A deficiency and by anoxemia were additive and therefore the lesions in the two cases are probably different. Anoxemia induced by CO poisoning is similar in its effect on the eye: the formation of carbon monoxide hemoglobin has the same effect on visual thresholds as an equal loss of oxyhemoglobin at high altitudes (McFarland, Roughton, Halperin and Niven, 1944). Inhalation of CO from a cigarette caused an appreciable increase in the percentage in the blood of carbon monoxide hemoglobin. These changes in visual threshold are all reversible by oxygenation.

Other papers on the same general problem have been published by McFarland and Halperin (1940) and McFarland, Halperin and Niven (1944, 1945). In 1940 McFarland and Forbes showed that hypoglycemia as well as anoxia affect light sensitivity of the retina, probably by slowing oxidative processes. "Consequently, the effects of anoxia may be ameliorated by giving glucose and the effects of hypoglycemia by inhaling oxygen." The relation between anoxia and brightness discrimination has been discussed by Hecht et al. (1946) and the respiratory effects upon visual threshold by Wald et al. (1942), both senior authors being specialists in visual physiology. Gellhorn and Hailman (1944) observed a parallelism between changes in visual function under anoxia and changes in the electroencephalogram. A rise in retinal arterial pressure occurs at low altitudes and then slowly disappears (Duguet and Bailliart,

1947). A fall in retinal arterial pressure under anoxia is charateristic of nontolerant subjects. Anoxia also prolongs the latent period between stimulus and visual after-image (McFarland, Rurvich and Halperin, 1943).

The occurrence of a restriction in the visual field at altitude was noted by Wilmer and Berens in 1918. Smith, Seitz and Clark (1946) showed quantitatively the development of the peripheral blind area (angioscotomata) at partial pressures of oxygen equivalent to an altitude of 10,000 ft. According to Houston (1947a) scotomata can also be produced by aeroembolism within the retinal arteries.

k. ACCLIMATIZATION TO ANOXIA. The immediate responses and adjustments of the body to anoxic anoxia have been briefly outlined above. Those adjustments that occur only slowly over a period of time at altitude or during intermittent flights to high altitude constitute acclimatization to anoxia. The reality of such acclimatization has been well established. Its features have been discussed by Haldane (1927), by Gemmill (1941) and by Houston (1947b). Comprehensive investigations of this phenomenon have been reported by Merény, Korényi and Gordon (1944), Houston (1946b) and Houston and Riley (1947) on man, and by Reynolds and Phillips (1947) on the rat. The latter authors observed a regression of adaptation on interruption of altitude exposures, leaving the animals less tolerant to anoxia than unexposed animals.

Keys, Matthews, Forbes and McFarland (1938) studied the individual variations in a group of 10 men in the ability to acclimatize to high altitude. They found that youth, slow pulse, low-normal blood oxygen capacity, low alveolar oxygen pressure, high alveolar carbon dioxide pressure and high alkaline reserve at sea level are favorable to acclimatization at high altitude.

Perhaps the most commonly observed and the most significant factor in acclimatization to anoxia is an increased oxygen carrying power of the blood, due to increased content of hemoglobin and of erythrocytes, accompanied by an increase in myohemoglobin (Hurtado, Rotta, Merino and Pons, 1937), but with no increased affinity of hemoglobin for oxygen (Hall, 1936; Aste-Salazar and Hurtado, 1944). Recent evidence of increased hematopoietic activity during acclimatization to altitude has been reported by Hurtado, Merino and Delgado (1945) and Lewis et al. (1943) in experiments on men and by Stickney and Van Liere (1942b) in studies on the dog. Ruff and Strughold (1942) have recorded the changing blood picture of a man who stayed for 2 months at altitudes varying from 13,000 to 23,000 ft. The hemoglobin content of the blood rose from 18.3 to 24.5 gms. per cent and the red cell count from 5.64 to 8.32 millions per cubic mm. On return to sea level these values returned to normal, the hemoglobin content within one month and the red cell count some time later. Other references of the same import are, on men, Sankaran and Rajagopal (1938), and Vannotti and Markwalder (1939), and, on guinea pigs, Gordon and Kleinberg (1937) and Jensen and Alt (1945). Continuous residence at an altitude of 11,000 ft.(Smith, Belt, Arnold and Carrier, 1924-25) increases in man the volume of plasma as well as of corpuscles.

In the dog, according to Stickney and Van Liere (1942a), "The usual delay in gastric emptying time produced by anoxia has been found to be gradually reduced in every case" during discontinuous exposure to pressures simulating altitudes from 12,000 to 18,000 ft.

ACCELERATION. Acceleration is not a factor in climatic stress, but it is a hazard in military and naval aviation and it may not be out of place to consider it briefly here. Wood, Lambert, Baldes and Code (1946) have discussed the effects of acceleration on the cardiovascular system: increased weight of blood and tissues, decreased blood pressure at head level, which are the key to the orderly pattern of changes in ear opacity, ear pulse and heart rate. The function of the cerebrospinal fluid in protecting the cerebral circulation against radial acceleration was studied in cats by Rushmer, Beckman and Lee (1947). The biochemistry of gravity shock, induced in rabbits by suspending them in the vertical position, was found by Nastuk (1947) to depend upon a circulatory deficiency leading to tissue hypoxia. "The data suggest that tissue hypoxia produced by suspension of the rabbit results in loss of energy-rich phosphate bonds of muscle, and in impairment of the mechanism which generates these bonds. Under these conditions, production of energy from carbohydrate metabolism may fall to levels insufficient to sustain the animal." Protective aids against exposure to acceleratory force were tested by Britton, Pertzoff, French and Kline (1947).

The effect of food and drink was found by Clark and Jorgenson (1945a, b) to increase G tolerance in human subjects. "The similarity in results between the ingestion of water and milk and food largely rules out hyperglycemic effects. Fluid and food ingestion increases cardiac output without evoking vasomotor mechanisms or displacement of blood from somatic tissues to the visceral organs; increase in intra-abdominal pressure remains as the only explanation of G protection." In another report, Clark, Gordiner, McIntyre and Jorgenson (1945) present the results secured on 3 human subjects on the effects of hyperglycemia, induced by sugar ingestion, and of hypoglycemia induced by insulin injection on G tolerance. Slight effects (0.2 G) only were noted. "The trend toward a slight positive effect of blood sugar concentrations on G tolerance suggests the possibility that extracellular sugar may, by acting as a substrate in anaerobic glycolysis alleviate somewhat the brief brain and retinal anoxia associated with the acute brain anemia induced by blood displacement during radial acceleration."

Effect Of Altitude On Nutrient Requirements. There seems to be little reason to expect, and scanty evidence to support, a belief that altitude and its associated low oxygen tension will disturb the nutrient requirements of man. The low oxygen supply at altitude will depress, rather than stimulate, metabolic processes, and, even more surely than a hot-humid environment, will discourage the performance of muscular work and lower the capacity for work. Bronshtein (1944) has reported that hypoxemia lowers the level of ascorbic acid in the blood of guinea pigs and hastens the development of scurvy on a normal diet.

The extensive dephosphorylation of the tissues that Greig and Govier (1943) have demonstrated in animals exposed to anemic anoxia or to anoxic anoxia may, according to Govier (1944), extend to dephosphorylation of cocarboxylase, which may be very largely involved and leads to a rise in the blood thiamine and probably an increased spill-over into the urine. The end result might be an increased thiamine requirement. Gusman et al. (1945) have noted a rise in the pyruvic acid content in the blood of aviators, somewhat in proportion to the altitude attained, an observation that ties in with the findings of Govier. The problem deserves further study.

Hyperventilation may increase the water requirements by expediting the loss of water from the respiratory passages. The increase may not, however, be large (Marshall, 1946; Matthews, 1932-3).

The Effect Of Dietary Modifications On The Tolerance To Anoxia: Animal Experiments.

1. FASTING. A critical test of the question whether tolerance to anoxia can be modified by diet, is to compare fasting with feeding of a well-balanced diet. This was done with rats by Leblond, Gross and Laugier (1943), who found that fasting for 12 to 24 hours definitely depressed resistance to anoxia, but that fasting prolonged beyond this period was accompanied by a recovery of resistance. What may be a second report of the same experiments was published by Laugier and Leblond (1943), with the same outcome. In the experience of Smith, Oster and Toman (1944), the underfeeding of cats increases greatly their resistance to low oxygen tension.

The livers of fasted rats, when exposed to an atmosphere of nitrogen for 70 minutes, showed a 75 percent depression in oxygen uptake, while the livers of fed rats showed only a 25 percent depression (Craig, 1943). Whether the glycogen content of the liver or some other factor in the experiment determined the results was not established. Mylon and Wilhelmi (1945) confirmed Craig's results on rats, using subsistence on a low-protein high-carbohydrate diet in comparison with fasting. On this diet, the liver glycogen is high (4 to 7 percent) and may be an important contributing factor to increased resistance to anoxia. Van Middlesworth (1944) has reported that liver glycogen of rats is reduced in anoxic anoxia even in the presence of excess blood sugar induced by sugar feeding. The marked hyperglycemia and glycosuria of glucose-fed rats under reduced oxygen pressure, accompanied by a diminished cardiac and liver glycogen, has been called a condition of "anoxic diabetes" by Van Middlesworth (1946). Under the same conditions, adrenalectomized rats exhibit a hypoglycemia (Van Middlesworth, 1944).

2. CARBOHYDRATE FEEDING. The effect of carbohydrate feeding on the resistance of animals to anoxia was studied as early as 1907 by Packard. Using minnows (Fundulus heteroclitus) as subjects and producing anoxia by placing the fish in unaerated sea water, he showed clearly that intraperitoneal injection of fructose, glucose or maltose, but not sucrose or lactose, definitely prolonged life during oxygen lack. On the other hand, the survival of Fundulus fasted prior to anoxia was not improved by the feeding of a high-protein food, mussels. The favorable effect of the monosaccharides is attributed to a type of anaerobic oxidation promoted by sugar, in which the sugar acts as a hydrogen acceptor in accordance with a theory of oxidation proposed by Mathews (1905). Many years later, Selle (1944) secured evidence that the marked tolerance of young rats to anoxia is due primarily to an anaerobic source of energy and that this source of energy is replenished by glucose administration and depleted by insulin. Following decapitation of the young rat, gasping of the isolated head may continue for 30 minutes or more. The injection of glucose into the rat prior to decapitation increases the survival of respiratory activity of the isolated preparation by 30 percent, while injection of insulin results in a slight to moderate reduction in the duration of the aerobic gasps, an effect than can be counteracted by glucose. Fazekas and Himwich (1943) have studied further the anaerobic development of energy from carbohydrate cleavage for the maintenance of cerebral function.

Britton and Kline (1945), working with rats, reported that glucose administration, especially parenteral, improves greatly the resistance of rats to low barometric pressure. Fully fed animals survived somewhat better than fasted controls, while insulin markedly reduced the ability to withstand anoxia. An item of incidental importance in this report is the observation that survival time under anoxia is inversely related to environmental temperature: for a 10° C. drop, survivals were increased about 50 percent. Smith and Oster (1946) noted with cats also that insulin decreases resistance to hypoxia, while decreasing post-hypoxic hyperglycemia, but they observed no general correlation between anoxic tolerance and post-hypoxic hyperglycemia. According to Himwich, Fazekas and Homburger (1943), hyperglycemia protects anoxic infant rats but not adults.

Studying the mechanism for the maintenance of life in the newborn rat during anoxia, Himwich et al. (1942) injected the animals with various substances modifying carbohydrate metabolism and noted the survival times after exposure to an atmosphere of nitrogen. Iodoacetate and insulin shortened the survival period, while glucose prolonged it considerably, demonstrating the importance of glucose in serving as a source of energy under anaerobic conditions.

Büsing and Kauff (1942) observed a slightly favorable effect of a prefeeding of fructose on the tolerance of rabbits to low air pressures. Prior observations of Büsing, and Forster (1940) had indicated a favorable effect of massive doses of vitamin B_1 on rabbits exposed to low oxygen tensions. These findings interested Büsing and Kauff in the effects of sugar and of thiamine on the blood creatine and creatinine, in view of the intimate relationship of creatine phosphate in the carbohydrate metabolism, particularly in muscle. It was found that on exposure to diminished pressure, equivalent to altitudes of 9500 to 10,000 m., the total creatinine of the blood increases during the first half-hour, and then falls, but not to its pre-exposure level. A prefeeding of fructose increases this elevation of total creatinine, while a prefeeding of vitamin B_1 depresses it. The whole picture conforms with the theory that anoxia disturbs the oxidation of carbohydrate, the disturbance being aggravated by sugar feeding and ameliorated by administration of vitamin B_1.

But the results of glucose administration on tolerance to anoxia in laboratory animals have not been concordant. Dohan (1942) tested the effects of high-carbohydrate and high-fat diets on the survival of adult rats exposed for 15.5 to 23 hours to air pressures ranging from 380 to 235 mm. Hg. Three of 8 rats fed the high-carbohydrate diet and 4 of 9 fed the high-fat diet survived until the end of the experiments. Exposure of the rats for more than 2 days to low pressures produced a significant increase in adrenal weight and a significant decrease in the weight of thymus and testes, but again no differential diet effects were noted. The authors state: ''However, in connection with the lack of effect of diet in our experiment it is well to point out the long time intervals between feedings.'' The rats were tube-fed a daily caloric supply adequate for the maintenance of body weight at atmospheric pressure but only in the intervals between low-pressure exposures.

In a series of 5 experiments reported by Ivy, Friedemann and Grodins (undated report), 170 male albino rats were exposed to lethal degrees of anoxia, one-half of the animals being fed 1 gm. of sucrose the hour before exposure. No protective effect was observed: There was 41 percent survival of the treated animals and 46 percent survival in the controls. The failure of carbohydrate to prolong life may be due to the amount given, the lack of detectable response of a very anoxic-resistant animal, or the masking of any favorable effect of carbohydrate upon the R.Q. by the increased need of oxygen in increased metabolism. Langwill, King and MacLeod (1945) also failed to notice a beneficial effect of 2 gms. of sucrose given to adult male rats prior to exposure to moderate degrees of anoxia. In these experiments anoxia induced a marked diuresis and an increased alkalinity of the urine.

3. PROTEIN AND FAT FEEDING. The effect of a dietary protein supplement (5 gms. of raw horse meat) on the survival of nearly mature adult rats when exposed to severe anoxia (5 percent oxygen, 95 percent nitrogen) was studied by Langwill, King and MacLeod (1945). The basal diet was a commercial mixed feed containing 26.2 percent protein and 5.4 percent fat. The meat supplement appeared to exert a slight detrimental effect on tolerance to anoxia: 6 of 15 rats on the unsupplemented diet survived, while only 2 of 15 survived on the supplemented diet. However, application of the X^2 test fails to establish any significant effect of the protein supplement (P = 0.17). Ivy, Friedemann and Grodins (undated) reported a somewhat similar test with larger numbers of rats in which a protein-free and a high-protein diet (48 percent) were compared; the results indicated clearly (P = ca. 0.017) by the same statistical test, a less favorable effect on survival to anoxia of the high-protein diet. But whether the difference is due to a variable protein intake or to a variable carbohydrate intake is not clear. In neither case is the total caloric intake given, although this may be a factor in tolerance to anoxia, as indicated in the discussion above.

Evidence of the effect of fat-feeding on tolerance to anoxia is conflicting and inconclusive. With 8 and 9 adult male rats to a group, Dohan (1942) was unable to detect a difference in this respect between a high-carbohydrate and a high-fat diet, the protein content remaining constant. On the other hand, the experiments of Hove, Hickman and Harris (1945), also involving small groups of rats, indicate that even 12 percent of fat in the diet of animals exposed to severe anoxia equivalent to about 170 mm. Hg total air pressure is definitely detrimental to survival. But again caloric intakes are not recorded.

4. VITAMIN SUPPLEMENTS. The hypertrophy of the adrenal gland induced by anoxia suggests that anoxia disturbs the metabolism of ascorbic acid, and that the physiological effects of anoxia may be alleviated by ascorbic acid administration. It is well established that ascorbic acid is intimately involved in adrenal function, the ascorbic acid content of the gland being extremely high. In fact, the vitamin was first crystallized from this source. From experiments on human subjects that will be discussed later, Krasno, Ivy, Atkinson and Johnson (1943) received the impression that exposure to altitude causes a retention of ascorbic acid in the body, which is later released during intervals between exposures. They investigated this possibility by exposing guinea pigs for 12 hours to a simulated altitude of 18,000 ft., after intra-muscular injection of 100 mg. of ascorbic acid. Control animals, similarly injected, were not exposed to diminished pressure. Two to 4 hours after decompression of the test group, the plasma ascorbic acid level in both groups was determined and a few hours later all animals were sacrificed. The ascorbic acid content of both blood plasma and muscle tissue was higher in the exposed animals. These experiments were considered as confirming the suggestion obtained from the observations on men, though in themselves they fail to indicate any possible favorable effect of ascorbic acid administration on tolerance to anoxia.

Experimenting with an animal, the albino rat (male and nearly full grown), able to synthesize ascorbic acid in its tissues, Langwill, King and MacLeod (1945) studied the excretion of the vitamin in the urine under conditions of mild anoxia induced by exposure at atmospheric pressure to a gas mixture containing 7.7 percent of oxygen and 92.3 percent of nitrogen for 2 or 3 hours. The subsistence diet was Purina Dog Chow, alone or with supplements of raw horsemeat or sucrose. Exposure to anoxia diminished the output of ascorbic acid in the urine in all groups and experiments, somewhat in proportion to the concommitant rise in urine pH. The nature of the dietary supplements seemed to have no effect on the magnitude of this reduction in urinary ascorbic acid. Although the suggestion is not directly made by the authors of this report, one may infer from their discussion that, if the decrease in

urinary ascorbic acid in anoxia may be interpreted as the result of a retention of the vitamin in the tissues, it may be considered a protective mechanism available to the animal against agents or conditions that suppress respiration of the central nervous system. In a brief note, Peterson (1941) reported that intraperitoneal administration of ascorbic acid (or of methylene blue) increased the resistance of rats and mice to low oxygen tensions, presumably, according to the author, by making oxygen more available to the tissues.

Hailman (1944) studied the effects of some of the water-soluble vitamins, particularly riboflavin, in modifying the disturbances in tissue functions and in intact animals induced by anoxia. The experiments were inspired by published evidence (Dietrich and Pendl, 1937) "that perfusion of the isolated frog heart with low oxygen concentrations causes a weakening of the contractions which are promptly restored by physiological oxygen pressure or by adding a minute quantity of riboflavin to the perfusion medium." Hailman failed to confirm this anti-anoxic effect of riboflavin, but obtained positive results with this vitamin in preventing the anoxic effects on the spontaneous rhythmical contractions of smooth muscle from the frog's esophagus. Large doses of the B vitamins to male rats did not, in his experience, prevent hypertrophy of the adrenal cortex when the animals were subjected to a pressure of 294 mm. Hg for 48 hours. "In a series of 12 experiments on 7 dogs it was found that riboflavin, 1 mgm. per kgm. given intravenously, prevented the depression of the linguo-maxillary reflex during the inhalation of low oxygen mixtures."

Rabbits exposed to air pressures equivalent to altitudes of 9500 to 10,000 m. show some slight favorable effect of a pre-feeding of fructose, and a further, and slight, favorable effect of thiamine feeding, according to Büsing and Kauff (1942). The increased tolerance afforded by the latter supplement is presumed to relate to the proper metabolism of the fructose supplement. Wolff and Karlin (1947) failed to find, in mice receiving a normal diet, any correlation between survival to low oxygen tension and the riboflavin content of the liver.

It is known that resistance to reduced atmospheric pressure is decreased by the administration of thyroid material and it is suspected that some of the vitamins exert an anti-thyrogenic effect. Hence, Charipper, Goldsmith and Gordon (1945) performed some experiments "to ascertain whether an abnormal vitamin intake, deficiency or overdosage, would influence the resistance of rats exposed to lowered barometric pressures..." Dietary concentrations of riboflavin, pyridoxine or pantothenic acid that were definitely deficient were without effect on tolerance to decreased pressure, as were also supplements of thiamine, ascorbic acid and calcium pantothenate to such deficient synthetic diets. On the other hand, a diet deficient in thiamine seemed definitely to increase tolerance, an effect that could be obliterated by the administration of 1 mgm. of thiamine shortly before low-pressure exposure, a most anomalous result. A restricted intake of a complete diet also favored increased resistance to anoxia. An increase in resistance to anoxia in thiamine deficiency was also observed with cats by Smith, Oster and Toman (1944), but the effect may have been caused by a decreased intake of food, which in itself was shown to be effective. If the tissue anoxia induced by hemorrhagic shock is analogous to that induced by low atmospheric pressure, the findings of Govier and Greer (1941) on dogs are at variance with those just discussed. These authors observed an increase in blood keto acids (which may include pyruvic, acetoacetic, d-ketoglutaric and oxaloacetic) in hemorrhagic shock; on thiamine administration the blood keto acids decreased and the survival time was prolonged.

The observations of Hove, Hickman and Harris (1945) on the favorable effect of d-tocopherol on tolerance to decompression seem clear-cut except for the possible disturbing effects of variable food intakes, the data for which were not reported. Given orally in physiological quantities to adult rats, the natural mixed tocopherols induced an increased survival to anoxic anoxia averaging 80 percent as compared with controls on an E-low and low-fat diet. The respective diets were fed for 2 to 3 weeks prior to decompression. Injection of massive single doses of alpha-tocopherol phosphate into guinea pigs on a rabbit chow diet greatly increased the survival time to anoxia, but no such effect was secured with rats.

5. CARROT FEEDING. In 1938 Campbell discovered that rats subsisting on a sole diet of carrots, either raw or boiled, could withstand anoxia much longer than on a normal diet, although losing weight. The correlation between weight loss and survival was not close, however. The factors underlying the beneficial effect of a carrot diet are considered by Campbell (1939) to be the low-protein content, the presence of fiber, the presence of gluta-

mine and of some unknown factor. The different proteinogenous amino acids were found to have variable effects on survival in low pressures. On the basis of his extensive experiments on rats, not readily interpretable nor very consistent among themselves, Campbell offers the following comment: "On the above evidence, suitable articles of diet for subjects exposed to the effects of oxygen want due either to disease or to high altitude are zein (but not whole maize), carrots, parsnips, beetroot, apples, bananas, starch, glucose, fat (lard), vitamins and salts. Gelatin and gluten (flour) might be used also in very moderate quantity and milk in small quantity."

This seems to be a rash extension to human nutrition of results obtained upon a laboratory animal, but has been quoted with approval by the British Medical Journal (Editorial, 1940), from which a more conservative attitude might be expected.

Campbell's results have been amply confirmed on the rat by Wetzig and D'Amour (1943), Nelson, Goetzl, Robins and Ivy (1943), Langwill, King and MacLeod (1945) and possibly by others. The results of the latter authors are particularly noteworthy. They found that when the consumption of dog chow by their experimental animals was regulated iso-calorically with the consumption of dehydrated carrots, animals on the two diets survived about equally well in severe anoxia (30 min. at 40,000 ft.) under some conditions of feeding, "but in other tests, with an opportunity for adaptation by repeated exposures and more gradual ascent, there was evidence of added protection as a result of the carrot diet. The increased alkalinity, high potassium content and low protein content of the carrot diet afford a tentative basis of accounting for the increased tolerance." The assumed favorable effect of a high potassium intake is based upon the findings of Dixon (1940) that, in cerebral cortex tissue in vitro, the addition of excess potassium ions markedly inhibits the production of lactic acid and the destruction of glucose resulting from oxygen deprivation.

6. MINERALS. In experiments at the Naval Medical Research Institute (1945) on the self-selection of water and salt in rats rendered anoxic by decompression at altitude, it was found that the voluntary intake of water and of salt was not altered by acute or chronic anoxia. The usually observed increase in heart rate in guinea pigs on decompression is lowered by administration of calcium salts, according to the report of Geppert, Pena and Schaefer (1944). Other evidence of a favorable effect of calcium on resistance to anoxia has been presented by Di Macco (1945), using guinea pigs also.

The well established stimulation to erythropoiesis induced by the cobaltous ion was found by Dorrance and others (1943) to be associated in rats with an increased work performance under conditions of anoxia, though in the small dosage used some untoward effects on the animals were noted.

The Effects of Dietary Modifications on Tolerance to Altitude: Human Experiments.

1. CARBOHYDRATE FEEDING. In 1940, Boothby, Lovelace and Benson, from theoretical considerations of the effect of high altitude on the human body, estimated that an aviator breathing the ambient air, and unacclimatized to altitude, can withstand an elevation of 15,000 ft. more than an hour; one of 20,000 ft., less than an hour. Since more oxygen is needed to burn fat than to burn sugar to CO_2 and H_2O (and in fact more oxygen per calorie of energy produced), it was estimated that a high-carbohydrate diet is capable of raising the aviation ceiling 1000 to 2000 ft. From considerations of the relation of the respiratory quotient to alveolar oxygen tension, Grodins (undated) computed that the aviation ceiling may be 2000 to 5000 ft. higher when the R.Q. is 1, that of pure sugar combustion, than when the R.Q. is 0.7, that of the combustion of pure fat.

The fact that sugar is the main (or sole) source of energy for the brain and that the brain responds adversely to hypoglycemia (as it does to anoxia) is merely another reason for favoring carbohydrate food in aviation. Polonovski (1940) observed that the ingestion at high altitude of 80 gms. of sugar helped in combating fatigue and the tendency to somnolence. A sugar drink, fortified with minerals, was found by Blasius and Bauereisen (1942) to compensate for the changes in carbohydrate metabolism induced by anoxia. Improvement in tolerance was also revealed by a writing test, by the clinical behavior and by the ability to tolerate longer an altitude of 7000 m. The improvement in tolerance seemed greater for those subjects, thirteen in all, whose tolerance to altitude was initially greater.

The relationship between the consumption of carbohydrate foods and tolerance to altitude was thoroughly studied during the war period in several laboratories throughout the country, generally in projects sponsored by the Committee on Medical Research of the Office of Scientific Research and Development. The results obtained are in good agreement and furnish a most impressive solution of the problem.

King, Bickerman and associates (1945) have reported the results of a very thorough study of the effect of the composition of pre-flight and in-flight meals on tolerance to altitudes of 15,000 to 17,000 ft. The acquired tolerance was measured by 13 separate tests, but in the interpretation of the data, two tests only were selected for primary emphasis, i.e., the block placement (University of Minnesota) test and angioscotoma records, as criteria of psychomotor performance and of corticoretinal function (chiefly peripheral vision), respectively. The report contains illustrative records comparing 6.5 hour fast with breakfasts and lunches carrying 600 to 800 calories and containing high proportions of carbohydrate, protein or fat. Diet groups of 10 men each were employed. Fasting beyond 4 to 5 hours was found to be least favorable to altitude tolerance and high-carbohydrate meals most favorable. Dietary protein increments from 10 to 20, 30 and 40 percent of the total calories were accompanied by decrements in altitude tolerance. Fats were intermediate in their effects. In terms of equivalent altitude (or gain in "ceiling"), carbohydrate showed a saving over protein of approximately 2000 ft. in the 12,000 to 17,000 foot range (King, 1946). The authors are careful to state: "These findings pertain to immediate pre-flight and in-flight feeding and do not connote departures from normal requirements or good practices relative to the food intake as a whole." The authors, in commenting on the advantages of carbohydrate foods, emphasize the importance of maintaining the glycogen reserves of the body at altitude. In a private communication, King expresses the opinion that the evidence of these experiments favors the view that carbohydrates, as compared to protein foods, also afford some protection against syncope at altitude. In a later publication, King, Bouvet et al. (1945), show that pre-flight carbohydrate meals hold their advantage for 6 hours over high-protein high-fat meals. In all of these tests the distortion in the test meals of the proportions of the various organic nutrients was rather extreme.

McFarland, Halperin and Niven (1945) found that anoxia (simulated high altitude) impairs the differential intensity thresholds for vision at low brightness levels, and that the ingestion of 50 gms. of glucose during exposure to low-oxygen tension results in a considerable decrease in the impairment due to anoxia. In 3 subjects this decrease amounted to 42, 25 and 48 percent. Under ground level conditions, sugar ingestion does not increase visual sensitivity in dim light. At altitude, the anti-anoxic effect of sugar on this function parallels the concentration of sugar in the blood, and seems to depend upon blood sugar level. From the work of King and of McFarland and their associates, one may conclude that anoxia restricts the field of peripheral vision and depresses visual sensitivity in dim light, and that with prior sugar feeding both impairments in visual efficiency are considerably lessened.

A possible adverse effect of sugar feeding prior to altitude ascent is pointed out by D'Angelo (1946b) who noted that the ingestion of glucose at moderate altitude "can cause the development [within a 10-hour period] of secondary hypoglycemic reactions similar to those induced at ground level, and sufficiently marked to affect adversely well-being and efficiency in flight." While sugar tolerance is not appreciably altered at moderate altitude (8000 to 10,000 ft.), "There is suggestive evidence...that the homeostatic mechanism controlling blood sugar level is affected."

The experiments of Eckman, Barach and others (1945), while involving fewer subjects and different criteria of tolerance, were similar in purpose and in outcome to those of King et al. The criteria in this case were changes in blood gases, in the composition of alveolar air and in psychomotor and psychological performance. Unfortunately, the validity of average changes in test measurement was not tested statistically, contrary to King's practice. The prescribed test meals contained 750 cals. each and were high in carbohydrate or high in both protein and fat. In some tests the subjects were permitted to choose the quantity and type of food consumed. Again, there was an indicated gain in altitude tolerance on the high-carbohydrate meal over the high-protein high-fat meal, estimated to range from 1000 to 2000 ft. at an altitude of 17,000 ft. It is important to note, however, that when the subjects were permitted to choose their pre-flight meals their altitude tolerance was decreased compared with the high-carbohydrate meals by only some 500 ft. The authors also comment on the fact that,

in so far as this increase in altitude tolerance induced by carbohydrate food is traceable to an elevation in the respiratory quotient, it would not be expected to appear under conditions of oxygen inhalation.

At the Smoky Hill Army Air Field at Salina, Kansas, Green, Butts and Mulholland (1945) reinvestigated the relationship of anoxia susceptibility to diet, using 50 subjects and exposures of 2 hours to a simulated altitude of 17,000 ft. without oxygen. The two pre-flight meals tested contained 69 percent carbohydrate, 21 percent fat and 10 per cent protein in one case and about equal proportions of these classes of organic nutrients in the other. The tests employed for the evaluation of anoxic effects were: a single dimensional pursuit test, a vision demonstration card test, an arithmetic test, a cube-placing test and an angioscotomata test. Statistical methods were used in interpreting the data secured. The advantages of the high carbohydrate meal were evident generally, although the magnitude of the indicated diet differences (ranging from 4 to 50 percent) and the degree of confidence in their reality differed. Contrary to the experience of King and associates, the angioscotomata test was the least sensitive to diet effects. In commenting on their findings, the authors say:

"In the operation of aircraft small differences in mental functioning and psychomotor co-ordination may produce errors in judgment and reaction responsible for inaccurate bombing, poor marksmanship or loss of the aircraft.

"Consideration of these factors suggests that the arithmetical advantages of high carbohydrate feedings may be indicative of more significant gains to be had in the form of safety and efficiency in flight." Subjective impressions of efficiency generally favored the high-carbohydrate meal although it was the less palatable.

The authors conclude: "Susceptibility to anoxia may be reduced by the feeding of diets high in carbohydrate prior to ascent. The magnitude of this effect is sufficient to justify its employment in the feeding of personnel engaging in flight under conditions of actual or anticipated lowered oxygen partial pressure."

A different approach to the problem of the relationship of diet to altitude tolerance was taken in the experiments of Riesen, Tahmisian and Mackenzie (1946). The distinctive features of their plan was to superimpose beverages containing 80 gms. of glucose, or simulated drink containing saccharine, to a diet of choice; 30 to 50 minutes after the supplemental beverage, the subjects were decompressed to 27,000 ft., where fulminating anoxia rapidly leads to unconsciousness and death; the oxygen masks were disconnected and the time till unconsciousness supervened was taken as the measurement of the effect of the supplemental feeding; unconsciousness was revealed by the inability to continue writing dictated ditties. Taking the pooled data from 39 tests without glucose and 38 tests with glucose, the prolongation of consciousness induced by glucose feeding averaged 73.5 seconds, representing an advantage of 39 percent over no glucose. The t value of 4.3 testifies to the high significance of the difference. At 30,000 ft. the advantage of glucose feeding, while significant at the 5 percent level, amounted to only 17 percent. When the tests are made 60 to 80 minutes after ingesting the test beverages, the sugar advantage is not evident for trained fliers but is still highly significant for untrained fliers. The authors note in this connection that the protection afforded by sugar against this extreme degree of anoxia parallels the blood sugar level.

In emphasizing the importance of their findings, Riesen et al. point out: "In critical situations such as bail out, loss of cabin pressure, or failure of oxygen systems additional seconds of consciousness can mean the difference between life and death."

The effect of diet, among other factors, on the incidence of decompression sickness at altitude was studied by Burkhardt et al. (1947). The experiments involved 7 subjects who were exposed to air pressures equivalent to 38,000 ft. of altitude 3 times weekly, approximately 1.5 hours after the evening meal. The daily diets contained about 3000 cals. and were high either in protein (280 gms.), fat (252 gms.), or carbohydrate (574 gms.), while the control diet was normal in composition. The average percentages of descents due to "incapacitating bends" on the total number of tests with 7 subjects were 69 for the control diet, 78 for the high-fat diet, 88 for the high-protein diet, and 58 for the high-carbohydrate diet. A favorable effect of a high-carbohydrate diet and an unfavorable effect of the high-fat and high-protein diets are indicated by these averages, but definite conclusions are not possible in the

absence of a statistical analysis. Judging from the averages recorded for each subject, it seems clear that the favorable effect of the high-carbohydrate diet was established; the unfavorable effect of the high-fat diet is not so clear. The authors offer no explanation or discussion of these differential diet effects and none occurs to the reviewers. To the extent that sugar feeding would increase the pCO_2 of the alveolar air, Lundbaek (1944), it would be expected, according to Hodes and Larrabee (1946), to increase susceptibility to bends, rather than decrease it. The conclusions of the authors are conservative: "These results show that a very high protein diet predisposes to descents due to bends and that a high carbohydrate diet has the opposite influence. Since these effects were observed with extremes in the diet, it is unlikely that ordinary dietary conditions have an appreciable influence on the susceptibility to bends." Age, altitude and exercise at altitude proved to be the most important factors which predispose to bends and chokes in aviators. A high-fat diet was the most effective procedure for reducing abdominal gas pains.

Human subjects exposed for 1 hour to an oxygen tension corresponding to an altitude of 4000 to 5500 m., excreted less urinary phosphate during the hour of exposure and the following hour (Beyne, Boy and Polonovski, 1944). Previous ingestion of 100 gms. of glucose had little effect on the phosphate excretion. Polonovski (1943) reported some slight effect of sugar, but the excretion of total base in the urine at altitude was not shown by Beyne, Boy, Leduc and Polonovski (1945) to be consistently modified by pre-feeding with sugar.

McFarland and Forbes (1940) have reported some very significant studies on the relationship of alveolar oxygen tension and blood sugar level to visual dark adaptation. The former was varied by varying the oxygen concentration in an experimental chamber maintained at about 70° F., with constant ventilation and constant total barometric pressure. The latter was varied by glucose ingestion or insulin administration. The background of the study is well stated by the authors in the following words:

"The functioning of the central nervous system appears to depend upon a continuous and adequate supply of oxygen and glucose. When the concentration of either of these substances in the blood is lowered to approximately one-half of its usual level, there is significant impairment in cerebral function. At one-third or one-fourth of the normal level, the individual lapses into coma. The effects of mild, intermediate, and severe degrees of anoxia on sensory and mental functions have been extensively studied. In the case of hypoglycemia, however, only the relatively severe effects have received attention, mostly in connection with the treatment of diabetes and more recently in relation to the insulin-shock treatment of schizophrenia."

Using 10 subjects varying in age from 25 to 37 years, and measuring light sensitivity with the Hecht adaptometer, both the rod and the cone portions of the dark adaptation curve were elevated by anoxia and by insulin, while the ingestion of glucose (70 to 80 gms.) largely counteracted the anoxic effect within 6 to 8 minutes. High correlations were demonstrated between changes in the visual threshold (Δlog I) and the alveolar oxygen tension (r= -0.89$\pm$ 0.03) and between Δlog I and the glucose concentration of the blood (r= -0.87 $\pm$ 0.04). The highest correlation was obtained between Δ log I and the product of alveolar pO_2 (mm. Hg) and the sugar concentration of the blood (mg. percent), with r = -0.95 $\pm$ 0.01. Again quoting the authors:

"The experiments reported above lend support to the hypothesis that both anoxia and hypoglycemia produce their effects on light sensitivity in essentially the same way; namely, by slowing the oxidative processes. Consequently the effects of anoxia may be ameliorated by giving glucose and the effects of hypoglycemia by inhaling oxygen. In our opinion, the changes may be attributed directly to the effects on the nervous tissue of the visual mechanism and the brain rather than on the photochemical processes of the retina."

2. VITAMIN FEEDING. The hope is so frequently entertained by nutritionists, even though it almost invariably ends in disappointment, that vitamins consumed above demonstrated requirements will exert some miraculous effect on body functioning in contrast to the more prosaic nutrients, the proteins, carbohydrates, fats and minerals. The hope seems to be based upon the presumption that if a vitamin promotes a given function in the body, more of it should do even a better job. This is merely one phase, or one implication, of a theory current in many quarters that there is a wide difference between adequate and optimal

nutrition. The controversy over the latter theory centers around the proper definition of "adequate nutrition," but also involves the interpretation of available evidence.

In vitamin A deficiency, the light sensitivity of the dark-adapted eye is impaired, and this impairment can be removed easily and quickly by dietary administration of vitamin A or of its precursors. The prevailing opinion, as expressed for example by Rowland and Sloan (1945) and Rose and Schmidt (1947), is that the visual acuity of the individual in dim light cannot be improved by vitamin A supplementation of an adequate diet. Prior evidence to the contrary may be questioned on one basis or another. Rowland and Sloan state the situation well: "It should be emphasized that true night blindness due to avitaminosis is undoubtedly an extremely rare occurence in otherwise healthy young men. Evidence from other studies shows, moreover, that in the vast majority who have normal night vision, no improvement results from the addition of vitamins to an already adequate diet."

The observation of McFarland, Halperin and Niven (1945) that anoxia impairs the light threshold for vision in dim light has been noted above. Since this impairment is corrected (partially or entirely) by prior glucose feeding, it seems unlikely that a pre-feeding of vitamin A would also exert an anti-anoxic effect, since the relation of sugar and of vitamin A to vision are so entirely different. McDonald and Adler (1939) showed the anoxic effect and the vitamin A effect on dark adaptation to be additive. King (1943) did not observe a significant disturbance in the concentration of vitamin A in the blood plasma during mild anoxia, the data secured being extremely variable.

The effect of ascorbic acid on altitude tolerance in man has been studied in a number of laboratories with rather inconsistent results. The experiments of Ivy and associates (see Krasno, Cilley, Boutwell and Ivy, 1945) at Northwestern University were concerned, among other things, with the effect on human subjects of the degree of ascorbic acid deficiency induced and of the disturbance of the metabolism of the vitamin by mild anoxia. Groups of 7 to 11 subjects were exposed repeatedly to 18,000 ft. without supplemental oxygen, and to 35,000 ft. with pure oxygen for 1 hour. The basal diet was adequate and contained about 90 mg. of ascorbic acid per day. During several weeks of repeated exposure to mild anoxia, the urinary output decreased from 34 mg. to 12 mg. per day, and the blood plasma level of the vitamin dropped from 0.73 to 0.58 mg. percent. These changes are interpreted as indicative of increased utilization of ascorbic acid in anoxia. On exposure of the men to 35,000 ft. with oxygen for one hour, the urinary excretion of ascorbic acid and the blood plasma level increased. The urinary excretion of total fixed base first increased at altitude, and then decreased, leaving the total output unaltered. In interpreting their findings, the authors state:

"In view of the role that ascorbic acid plays in cellular oxidation-reduction reactions, its presence normally in a relatively high concentration in the adrenals, and the observation that the vitamin may be depleted by repeated exposure to anoxia, which also depletes body base, it is suggested that liberal quantities of fruit or fruit juices be supplied in the diet of aviators and patients who may be subject to exposure to discontinuous or continuous anoxia."

It has been suggested that the decreased content of ascorbic acid in urine during anoxia may be a result of destruction of the vitamin in the bladder by an alkaline urine. Under the conditions of his experiments, King (1943) noted only slight disturbances in acid-base excretion and the urinary output of ascorbic acid in anoxia.

Lucas (1944) has reported the response of human subjects to 1 gram doses of ascorbic acid administered just prior to exposure to a simulated altitude of 40,000 ft. for periods of 10 to 20 minutes. The effect on the composition of alveolar air, the occurrence of bends, the performance of the ball test and the writing test, and the general behavior of the subjects was recorded. No distinct advantages of ascorbic acid dosage were noted. If any improvement occurred it was slight at this altitude and insufficient "to justify its administration at present to high flying air crew." The extensive experience of Riesen, Tahmisian and Mackenzie (1946) on the use of pre-flight ascorbic acid beverages, either with or without added sugar, was also quite negative: the vitamin in amounts of 1 gm. exerted no demonstrable effect on the duration of consciousness at 27,000 to 30,000 ft.

Experiments with members of the vitamin B complex in relation to altitude tolerance have been generally negative in significance. King (1943) reported no significant changes at

altitude (15,000 to 17,000 ft.) in the blood plasma values or the urinary excretion of thiamine, nicotinic acid, riboflavin and pantothenic acid. In the experiments of Hailman (1944), the daily oral administration of large doses of thiamine, riboflavin, nicotinamide, pyridoxine and pantothenic acid for a period of 3 weeks did not prevent (in 4 adult human subjects) changes due to anoxia in the critical fusion frequency of flicker, the electroencephalogram, or the pulse rate.

A more systematic attack on the problem of the relationship between the vitamins of the B complex and tolerance to anoxia was made at Northwestern University and reported by Friedemann and Ivy (1947) and Harris, Ivy and Friedemann (1947). A group of 7 young men were put upon a well-balanced diet except that the dietary intakes of thiamine and riboflavin were restricted to 0.85 mg. and 0.95 mg. daily, respectively. While these amounts of the vitamins are much smaller than the recommended allowances of the Food and Nutrition Board of the National Research Council, the subjects remained in good health on this diet for 4 to almost 7 months without any evidence of physical deterioration as measured by physiological responses to standard exercises on the bicycle ergometer, with bar-bells and with dumb-bells, by clinical observations and by analyses of blood and urine.

Exhaustive work (6.6 to 7.7 cals. per min.) on the bicycle ergometer was performed twice each week at a simulated altitude of 15,000 ft. and three times weekly at ground level. Although the work capacity of the men on the basal diet averaged at altitude only 60 percent of that at ground level, increasing supplementation of the diet with thiamine and riboflavin up to 2.75 to 3 mg. daily afforded no improvement.

The authors concluded that "Thiamine or riboflavin restriction or supplementation had no apparent effect on the work output in any of the subjects."

Another interesting observation is described by the authors of this report as follows: "Training did not apparently increase the tolerance to anoxia at comparative rest. However, the observations on the height and rate of return of the pulse rate, together with the data on the work output, point definitely to an increased tolerance to anoxia during and immediately after work as the training progressed.

"Our observations demonstrate that a program of physical training conducted at ground level can contribute to increased efficiency for work at high altitude. They suggest that such a program of training may in a measure take the place of acclimatization in mountainous regions."

Food Acceptance At Altitude. The problem of rationing aviators and troops stationed at high altitude is not by any means determined solely by nutritional considerations. As Dove (1946) well says: "Each food must be evaluated not by what it possesses but by what it gives to the consumer; and it gives to the consumer in gross value its per cent value per unit weight times the weight of food accepted."

Experiments on human subjects reviewed above have shown conclusively the value of carbohydrate foods consumed prior to or during flight in raising altitude tolerance. But unfortunately in actual practice the problem is not so simple. Quoting from an unpublished manuscript (1946) issued by the Army Air Force entitled "Diet in relation to pilots fatigue:" "Diets high in carbohydrate and very low in protein are not particularly the type that have the most appetite appeal....Actual tests made in feeding air crews these high carbohydrate low protein menus showed very poor consumption of the high carbohydrate foods...variety and quality of the high carbohydrate food items may increase their acceptability...In the meantime the inclusion of high carbohydrate 'snaks' such as the 'Air Crew Lunch' is a step in the right direction."

The factors affecting food preferences have been discussed by Eppright (1947) and some of the characteristics of human appetite by Goetzl and Stone (1946). Approaching the latter subject experimentally, the authors observed a definite correlation of threshold values of the sense of smell, one factor in appetite, with the energy content of the food consumed: "...in all subjects and at all times meals were preceded by a period of significantly declining and followed by one of significantly rising threshold values of the sense of smell."

But the pertinent problem for this section of the report is that concerned with the effect of altitude and anoxia on appetite and food acceptance. The Naval Medical Research Institute (1945) has reported experiments designed to ascertain "whether rats will select an optimal diet with respect to salt for the satisfaction of nutritional requirements under conditions of altitude anoxia." No difference was noted between the intake of salt (or of water) at ground level and at altitude. Gellhorn and Hailman (1943) in their discussion of the effect of anoxia on the sense organs cite data by Hingston (in turn cited from Barcroft) indicating a diminution of taste sensations and inability to taste onions and peppermint at an altitude of 16,500 ft. Friedemann (undated) has made further citations from the experiences of Major Hingston as medical officer of the Mount Everest Expedition of 1924. The general opinion of this expedition was that sweet things were the most palatable and meat the least palatable at 19,000 ft.

Green and Butts (1945) studied the factors affecting acceptability of meals served in the air by noting the relative consumption of 100 food items contained in some 10,000 meals served at altitude and compared the findings with those secured with the same items served at ground level. "...the highest acceptability aloft is possessed by baked goods and desserts. Soups, beverages and meats show roughly equal consumption in both environments. Salads, potatoes and vegetables have air acceptability about 80 percent of that on the ground....Bread-stuffs and desserts, however, since they are palatable even when cold, often were eaten when the mission was too short to allow heating of the remainder of the meal....Even so, the con-sumption of breads and desserts on individual long missions...was equal to, or better than that observed on the ground....Food is regarded much more critically in the air. Minor alterations in taste, odor and appearance considerably affect acceptability. Consequently, great attention must be paid to skilled preparation, flavor and eye appeal."

The problem of the peculiar features of menu selection for aviators is discussed by Weaver and others (1947) and by Armstrong (1943) with less obvious association with quanti-tative observations of food preferences in the air as contrasted with those on the ground. Crocker's book (1945) on flavor discusses the effect of serving foods hot or cold on flavor and acceptability.

Published Russian experiences indicate that the fat components of the diet of aviators should be restricted (Vladimirov et al., 1945), and emphasize the diminution of appetite at altitude, the early loss of appetite for meat and the continuing appetite for sweets (Krotkov, 1947). A supplement of acid fruit is recommended.

The Effect Of Drugs On Altitude Tolerance. The effect of Drugs on altitude tolerance is not an integral part of the subject matter of this report, but much material (not at all exhaustive) of this description was collected incidentally in the course of our literature coverage. Since it may be of value to the readers of the report, it has been condensed in tabular form and present-ed without further comment.

Table 2.

**Effects of Treatments Other Than Nutritional on Altitude
Tolerance, Including Massive Vitamin Dosages**

Treatment	Subject or Substance	Remarks	Reference
Drugs			
Aminophyllin + demerol	Man	Failed to alleviate or prevent decompression sickness	Williams et al. (1946)
Ammonium chloride	Man	Increased tolerance 1 to 2 days after ingestion	Barach et al. (1946)
	Man	Beneficial effects of ammonium chloride + O_2 were additive	Barach et al. (1947)
	Man	Failed to prevent mountain sickness	Barron et al. (1937)
	Rabbit	Prevented death from aeroembolism	Catchpole and Gersh (1946)
	Man	Caused a gain of 1000 to 2000 m. in altitude	Christensen and Smith (1936)
	Man	Better performance at altitude	Douglas et al. (1933)
	Dog	Adaptation to conditions of low O_2 pressure took place quickly	Goebel and Marczewski (1938)
	Man	Gastric secretion of HCl uninfluenced at altitude	Hartiala and Karvonen (1946)
	Man	Work capacity at altitude improved	Hartmann and von Muralt (1934)
	Man	Reduced incidence of incapacitating symptoms of decompression sickness in some but not all susceptible persons	Hodes and Larrabee (1946)
	Rabbit	Produced marked resistance to O_2 deficiency	Isikawa (1939)
	Man	Improved carbohydrate oxidation in anoxia	Ivy et al. (undated report to O.Q.M.G.)
	Man	Increased tolerance to low barometric pressure	Margaria and Faraglia (1940)

Treatment	Subject or Substance	Remarks	Reference
Ammonium chloride (cont)	Man	Increased altitude tolerance indicated	Rühl (1943)
Amphetamine or benzedrine	Man	Significantly decreased incidence of intolerable bends	Ivy et al. (1943)
Amphetamine + O_2	Man	Eradicated intolerable bends; markedly reduced incidence of bends	Ivy et al. (1943)
Amphetamine or benzedrine	Rat	Increased resistance as indicated by the EEG in moderate anoxia	Kessler et al. (1943)
	Man	No demonstrable value in preventing swing-sickness (simulating airsickness)	Smith (1946d)
Army Motion Sickness Remedy (Na amytal atropine sulphate and scopolamine hydrobromide)	Man	Seemingly no more effective than its content of atropine and scopolamine in preventing swingsickness	Smith (1946d)
Aspirin	Man	Time at altitude prolonged	Burkhardt et al. (1947)
	Man	Decreased the incidence of bends	Ivy et al. (1943)
	Man	No significant change in incidence of decompression sickness	Thompson et al. (1944)
Aspirin + codeine	Man	Failed to alleviate or prevent decompression sickness	Williams et al. (1946)
Atropine-Sulphate	Man	Increased the incidence and severity of pain due to intestinal gas	Blair et al. (1947)
Atropine-Sulphate	Man	Effective in preventing swingsickness	Smith and Hemingway (1946)
Benzoyloscine	Man	Moderately effective in preventing swing-sickness	Smith and Hemingway (1946)
Benzoyltropine	Man	Moderately effective in preventing swing-sickness	Smith and Hemingway (1946)
Codeine	Man	Average time at altitude was prolonged	Burkhardt et al. (1947)

Treatment	Subject or Substance	Remarks	Reference
Coramine and similar drugs	Man	No effect upon tolerance to anoxia	Rühl (1943)
Demerol	Man	Average time at altitude was prolonged	Burkhardt et al. (1947)
Demerol	Man	Negligibly effective in preventing swingsickness	Smith and Hemingway (1946)
Digitalis	Rat	Gave no relief to anoxic symptoms	Campbell (1938)
Dilantin sodium	Rat Mouse	Enabled ceiling to be raised an average of 18 mm. Hg. Prolonged survival of mice at 150 mm. Hg.	Hoff and Yahn (1944)
Hematropine	Man	Moderately effective in preventing swingsickness	Smith and Hemingway (1946)
Hyocyamine hydrobromide	Man	Effective in preventing swingsickness	Smith and Hemingway (1946)
Hyoscine-HBr	Man	Potent preventative of airsickness	Lilienthal (1945)
Hyoscine	Man	Moderately effective in preventing air sickness	Smith (1946b, c)
Methyl atropine nitrate	Man	Slightly decreased intestinal gas	Blair et al. (1943)
8-Methyl caffeine	Man	Increased visual acuity for 60 to 80 min. at low pressure and low visibility	Streltsov (1944)
Methylene blue (+ O_2 breathing)	Man	O_2 saturation of blood increased	Brooks (1945)
Methylene blue	Dog	Restored altitude tolerance, lost by administration of Na nitrate	Lawson (1942)
Methylene blue	Rat Mouse	Increased resistance of both animals to anoxia	Peterson (1941)
Methylene blue	Man	Showed no effect upon altitude tolerance	Rühl (1943)
Morphine	Man	Physiologic importance still difficult to assess	Peterson et al. (1945a)

Treatment	Subject or Substance	Remarks	Reference
Morphine	Man	Effective in relieving decompression pain	Smith (1946a)
Nembutal	Rabbit	Muscular immobilization produced tended to favor survival	Catchpole and Gersh (1946)
Papaverine	Man	Increased the incidence and severity of pain due to intestinal gas	Blair et al. (1947)
Papaverine	Man	No significant changes in the incidence of decompression sickness	Thompson et al. (1944)
Pavatrine	Man	Of doubtful value in preventing swingsickness	Smith and Hemingway (1946)
Phenacetin	Man	Time at altitude prolonged	Burkhardt et al. (1947)
Prostigmine-Br	Man	Increased the incidence and severity of pain due to intestinal gas	Blair et al. (1947)
Scopolamine	Man	Effective in preventing swingsickness	Smith and Hemingway (1946)
Scopolamine + chlorobutanol + benzedrine	Man	Insignificantly more effective than scopolamine in preventing swingsickness	Smith (1946d)
Scopolamine + neostigmine	Man	Less effective than scopolamine in preventing swingsickness	Smith (1946d)
Scopolamine + thiobarbiturate	Man	Did not increase effects of scopolamine in preventing swingsickness	Smith (1946d)
Sodium barbital	Man	No demonstrable value in preventing swingsickness	Smith (1946d)
Sodium bicarbonate (given with ammonium chloride treatment)	Man	Alleviated symptoms of acidosis produced by the chloride	Barach et al. (1946)
Sodium bicarbonate	Rabbit	Ineffective in protection against aeroembolism	Catchpole and Gersh (1946)

Treatment	Subject or Substance	Remarks	Reference
Sodium bicarbonate	Man	Blood lactic acid, lowered at high altitude, invariably higher than when NH_4Cl is administered	Hartmann and von Muralt (1934)
Sodium bicarbonate	Rabbit	Animals less apt to become acclimatized to O_2 deficiency than normal or NH_4Cl treated ones	Isikawa (1939)
Sodium bicarbonate	Man	Produced alkalosis causing decreased resistance to anoxia	Margaria and Faraglia (1940)
Sodium ethylallyl thiobarbiturate (V-5)	Man	No demonstrable value in preventing swing-sickness	Smith (1946d)
Strophantin	Rat	No change in tolerance to altitude	Campbell (1938)
Sulfonamide drugs			
Sulfadiazine	Man	No effect upon susceptibility to swing-sickness	Smith (1946d)
Sulfanilamide	Dog	Increased tolerance	Lawson (1942)
Sulfanilamide	Man	Lowered an aviator's ceiling by some 5,000 ft.	Mackie (1939)
Sulfathiazole	Man	Failed to significantly alter ability to withstand effects of altitude	Peterson et al. (1945b)
	Man	No limitation of performance	Meister and Hestermann (1940)
Yohimbine	Man	No effects noted on ECG, muscle action potentials or heart rate	Geppert et al. (1944)
Enzymes			
Cytochrome c	Guinea pig less than 1 day old	No aid in artificial resuscitation of animals having gone through cycle of hyperpnea, convulsions and slow gasping respirations	Benjamin (1948)

67

Treatment	Subject or Substance	Remarks	Reference
Cytochrome c	Rat	Ineffective in prolonging survival time	Christiansen and Clinton (1947)
	Rat	Marked increase in liver erythrocytes and hemoglobin; increased liver regeneration noted	Drabkin (1947)
	Rat	No effect on survival time to anoxia	Michel and Scheinberg (1947); Scheinberg and Michel (1947)
	Rat decapitated after 8 min. in 3 pct. O_2 subsequent to injection	No effect noted upon hydrolyzable phosphate in kidney and heart tissues	Miller et al. (1948) c.f. Potter (1947)
	Rat Dog Man	Prevented decrease of tissue hydrolyzable P in rats, the ECG effects of anoxia in man, and the irreversible state in hemorrhagic shock in dogs	Proger and Dekaneas (1946); Proger et al. (1945a, b)
Adrenal and Pituitary Hormones			
Adrenaline	Heart-lung preparation	Caused rapid breakdown of glycogen in anoxia	Bogue et al. (1939)
	Guinea pig	Lowered tolerance to altitude of 9500 m.	Bronshtein (1944)
	Rat	Gave no relief to symptoms of anoxia	Campbell (1938)
	Rabbit	Increased anoxic hyperglycemia	Gellhorn and Packer (1939)
	Rabbit Rat	Reduced effectiveness upon blood sugar in prolonged anoxia	Gellhorn and Packer (1940); Malméjac (1946); Van Middlesworth et al. (1944)
	Chloralosed and bivagotomized dog	At pressures above 9000 m. hypertensive action of adrenaline decreased unless O_2 given, then not evident until 14,000 ft. attained	Hermann and Jourdan (1941)

Treatment	Subject or Substance	Remarks	Reference
Adrenaline	Nembutalized cat	No significant rise in resistance time to anoxia, or in post-hypoxic blood sugar values	Oster and Smith (1947)
	Man	Produced no significant change in incidence of decompression sickness	Thompson et al. (1944)
17-hydroxycorticosterone	Man	No significant change in altitude tolerance	Clinton et al. (1946)
Adrenal cortical extract	Experimental animals	Decreased mortality rate at altitude	Armstrong and Heim (1938)
Adrenal cortical extract or desoxycorticosterone acetate	Small animals	No significant effect noted on work performance at altitude	Dorrance et al. (1942)
(1) Adrenal cortical extract (2) Desoxycorticosterone acetate; (3) 17-hydroxycorticosterone; (4) 15 pct. Na succinate	Rat	(1) Survival rate greatly increased; (2), (3), (4) did not increase survival rates	Thorn et al. (1945)
Cortin	Rabbit	Resistance to anoxia not increased	Gorelov (1939)
Eucortone	Rat	Gave no relief to anoxic symptoms	Campbell (1938)
Adrenocorticotropic hormone	Rat	Exercised a beneficial effect upon resistance	Li and Herring (1945)
Pituitary extract	Rat	No change in tolerance to anoxia	Campbell (1938)

Thyroid Hormones and Endocrine Depressants

Treatment	Subject or Substance	Remarks	Reference
Thiouracil	Rat	Increased survival; O_2 consumption decreased 30 pct. in 21 days; red cell and white cell count reduced	Gordon et al. (1945)
	Rat	Increased tolerance to anoxia	Hughes and Astwood (1944)
	Mouse	No effect upon resistance	Kuznets and Streltsov (1947)
Thiourea	Mouse	Increased survival time	Gardner and Forbes (1945)

Treatment	Subject or Substance	Remarks	Reference
Thiourea (1) 0.5 pct. for from 4 to 30 days or (2) 200 mg. injected 5 hrs. prior to flight	Rat	(1) Increased tolerance; (2) no apparent benefit	Gordon et al. (1944)
Thyroidectomy	Rat	Increased resistance to anoxia	Herrlich et al. (1941)
(1) Thyroidectomy; (2) Thyroidectomy + thyroxine treatment; (3) Dinitrophenol; (4) 1 pct. solution of thiourea	Rat	No difference in tolerance between intact and operated fasted rats in (1); rats in (2) and (3) showed decreased resistance; rats in (4) showed marked increase in tolerance	Leblond (1944)
Thyroxine	Rat	Enhanced O_2 deficiency at 24° C.	Campbell (1938)
Miscellaneous			
Acetylcholine	Intestinal tissues of guinea pig and rabbit, cerebral tissues of cat	Indication of a correlation between acetylcholine content of tissue and resistance to anoxia	Welsh and Hyde (1944) also, c.f. De Michele and Scoz (1944)
Carbon dioxide - oxygen mixtures			
	Rat	Most effective in combination with glucose feeding	Britton and Kline (1945)
	Rabbit	Failed to prevent aeroembolism	Catchpole and Gersh (1946)
	Man	Adequate O_2 pressure maintained in lungs, blood and tissues in mild anoxia	Consolazio et al. (1947)
	Mouse Man	Did not increase altitude ceiling in mice above that with pure O_2; did not increase cardiac output in man	Fenn (1944)
	Man	Improved general well-being and capacity for work	Garasenko (1944)
	Man	Greatly alleviated or completely offset anoxic effects	Gellhorn and Hailman (1944)

Treatment	Subject or Substance	Remarks	Reference
Carbon dioxide - oxygen mixtures			
	Man	Added CO_2 permitted maximum utilization of available O_2 in anoxia	Gibbs et al. (1943)
	Rat	Lowered minimum altitude tolerance to aeroembolism	Harris et al. (1945)
	Man	No advantage on cerebral O_2 tension over pure O_2	Himwich et al. (1942)
	Man	Not significantly superior to pure O_2 in alleviating intolerable bends	Ivy et al. (1943)
Carbon dioxide + d-amphetamine	Man	Eradicated intolerable bends and markedly reduced total incidence	Ivy et al. (1943)
Carbon dioxide	Dog	Produced respiratory depression in anoxia	Ivy et al. (1947)
	Man	Altitude tolerance increased	Keys et al. (1943)
	Cat	Increased altitude tolerance	Kline (1947a, b)
	Rat liver	Reduced the effect of anoxia on adrenal-hepatic system	Nims et al. (1946)
	Man	Increased tolerance to altitude indicated	Rahn and Otis (1947)
	Man	Improved tolerance to altitude	Rühl (1943)
	Rat	Increased tolerance to 37,000 ft.	Van Middlesworth (1944)
Citric acid	Man	Reduced somewhat the effects of anoxia	Molchanova (1941)
Hemoglobin	Man	Transfused group at altitude of 10,200 ft. equal in performance to untreated group at sea level	Pace et al. (1947)
Lactic acid	Rabbit	Prevented death from aeroembolism	Catchpole and Gersh (1946)

Treatment	Subject or Substance	Remarks	Reference
Vitamins			
Vitamin A or Carotene	Rat	No aid in combating effects of anoxia	Campbell (1938)
Vitamin A or Carotene	Man	No effect upon visual threshold or rate of dark adaptation	Hartline (1946)
Vitamin A + other vitamins	Man	In vast majority of men having normal night vision, no improvement gained by supplementation	Rowland and Sloan (1945)
Vitamin B complex			
Nicotinic acid (or xanthine in doses similar to nicotinic acid)	Rat	Gave no relief to symptoms of anoxia	Campbell (1938)
Pyridoxine	Man	No demonstrable value in preventing motion sickness	Smith (1946d)
Riboflavin	Rat	Gave no relief to symptoms of anoxia	Campbell (1938)
Thiamine	Man	Gave no relief to gas pains	Blair et al. (1943)
	Rabbit	Increased resistance to anoxia	Bülsing and Kauff (1942)
	Rat	Gave no relief to symptoms of anoxia	Campbell (1938)
	Man	No demonstrable value in preventing swing-sickness	Smith (1946d)
Thiamine + metropine	Man	No incidence of discomfort due to intestinal gas	Blair et al. (1943)
Vitamin C	Rat	No beneficial effect on tolerance to altitude	Campbell (1938)
	Man	If of any benefit, it was slight	Lucas (1944)
Vitamin C	Mouse Rat	Increased resistance to low O_2 tension	Peterson (1941)

Treatment	Subject or Substance	Remarks	Reference
Vitamin C	Man	Had no demonstrable effect on duration of consciousness either alone or given with glucose	Riesen et al. (1946)
	Experimental animals	Increased altitude tolerance	Rühl (1943)
Vitamin D	Rat	No beneficial effect on tolerance to altitude	Campbell (1938)
Vitamin E	Guinea pigs Rat	Greatly increased survival to anoxic anoxia on guinea pigs; no such effect upon rats	Hove et al. (1945)

Conclusions. The effects of altitude on animal metabolism are due predominantly to a diminished partial pressure of oxygen in the inspired air and in the alveolar air. The anoxia thus produced may not affect the basal metabolic rate appreciably, though the evidence is conflicting on this point, nor the efficiency with which muscular work is done, but it clearly depresses the mental faculties, the acuity of sensory impressions, the will to work, the endurance of working and the work capacity. The respiratory effort required to transfer a unit of oxygen from the ambient air to the alveoli is of course increased, and the hyper-ventilation induced will increase to some extent the evaporation of water from the respiratory passages. Under greatly diminished partial pressures of oxygen the renal function and the motor, secretory and absorptive functions of the gastrointestinal tract may be impaired. The metabolism of carbohydrates is definitely disturbed, though the experimental evidence as to the direction or the extent of the disturbances is not unequivocal, except possibly for the induction of a lactacidemia.

These disturbances in body functioning induced by anoxic anoxia are not known to increase nutrient requirements with the possible exception of water, and here the increase would not be considerable. There are suggestions that the requirements for ascorbic acid and for thiamine may be increased, but there is nothing approaching a demonstration.

Certain dietary alterations in pre-flight and in-flight meals have been shown to increase tolerance to altitude, equivalent in human subjects at altitudes of 15,000 to 17,000 ft. to about 2000 ft. This increase in tolerance relates to the difference between high-carbohydrate and high-protein meals. The difference in altitude tolerance associated with prescribed high-carbohydrate meals and freely chosen meals is much less than this. The ingestion of carbohydrates as compared with protein foods immediately before and during flight to altitude increases mental efficiency, neuromuscular coordination, the capacity for muscular work, the field of peripheral vision, and the acuity of vision in dim light. It defers syncope for a longer time and decreases the severity of the symptoms of decompression sickness.

Vitamin supplements to an adequate diet have not been shown to be effective in increasing tolerance to anoxia. In particular, vitamin A supplements to an adequate diet have not been shown to increase light sensitivity in the dark adapted eye, nor should such an effect be expected since the anoxic impairment in light sensitivity in dim light seems to relate to a different mechanism than the rhodopsin cycle in which vitamin A is involved. Ascorbic acid supplements and supplements of the vitamins of the B complex have not been shown to be effective anti-anoxic agents in man.

The relation of foods to abdominal gases and abdominal gas pains at altitude is not as simple as it might seem. Foods containing difficultly digestible carbohydrates that may be

73

expected to ferment in the lower levels of the intestinal tract should, one would presume, be avoided in pre-flight or in in-flight meals, but not all such foods have been shown to give trouble. Blair's extensive studies show that the only consistent relation of gas discomfort to particular items of a freely chosen diet is found with carbonated water drunk prior to flight and with the consumption of melons. Extreme variations in the proportions in the diet of proteins, carbohydrates and fats have revealed less gas discomfort at altitude when the carbohydrate content is kept at a low level. Behnke (1941-2) believes that efforts toward the prevention of this condition should be directed toward the limitation of air swallowing, by limiting gum chewing, for example.

The favorable effects of carbohydrate foods on altitude tolerance does not indicate that an alteration in the day's menu is necessary. The desired result can be accomplished by a shift in the usual planning of meals such that meals taken prior to flight or in flight include a high proportion of sugars and sugar-yelding foods, leaving the high-protein and high-fat foods largely to post-flight meals. In fact, in view of the apparent preference of men for sweet foods at high altitudes and their distaste for high-protein foods, free choice meals may serve the purpose. Candy snacks, preferably sugar candy, might be wisely provided for prolonged flights.

It should be noted in particular that the favorable effects of carbohydrate foods on tolerance to anoxia have been observed under conditions of air breathing but at altitudes where normally pure oxygen would be provided. There is some reason to believe that much of the favorable effects of carbohydrate foods would not be evident during oxygen inhalation except at very high altitudes. Direct investigation of this problem is needed.

The experiments on animals concerned with altitude tolerance and its modification by dietary means are often conflicting among themselves and in contrast to human experience. As an example, the unanimously favorable effects of carbohydrates observed on human subjects have, as often as not, not appeared in animal experiments. These discrepancies indicate either that the technique of animal experiments of this type is imperfect, or that information secured on animals is frequently inapplicable to man, or both. A common fault in animal experiments is to disregard, and to leave uncontrolled, the food intake of the experimental animals, in spite of the fact that the level of food intake, particularly when inadequate, is (and has been shown to be) an important determinant of altitude tolerance.

V. LITERATURE CITED

Adolph, E. F. 1923. The nature of the activities of the human sweat glands. Am. J. Physiol. 66: 445-452.

_____ 1933. The metabolism and distribution of water in body and tissues. Physiol. Rev. 13: 336-71.

_____ 1938. Heat exchanges of man in the desert. Am. J. Physiol. 123: 486-99.

Adolph, E. F. and associates. 1947. Physiology of man in the desert. New York: Interscience, 357 pp.

Adolph, E. F. and A. H. Brown. 1943. Survival time of men without water in the desert. OEMcmr-206, Interim Report No. 8 to Com. Med. Res., O.S.R.D., May 25, 6 pp.

Adolph, E. F. and G. W. Molnar. 1946. Exchanges of heat and tolerances to cold in men exposed to outdoor weather. Am. J. Physiol. 146: 507-37.

Aggazzotti, A. 1923-4. Il limite di assimilazione del glucusio in alta montagna. (Limits of assimilation of glucose on high mountains.) Arch. Sci. Biol. 5: 1-21.

Albagli, B. 1939. O Metabolismo Básico em Funcão da Alimentacão e do Clima. (The basal metabolism as a function of nutrition and of climate.) Rio de Janeiro, Brasil. Livraria Atheneu, Jose Bernades, 167 pp.

Albergo, V. 1932. Metabolismo basale ed axione dinamico-specifica degli alimenti nei vecchi. (Basal metabolism and specific dynamic action of foods in old age.) Minerva Med. 2: 678-82.

Alekseev, S. G., G. E. Vladimirov, M. A. Kuntsevich and A. F. Panin. 1945. Specific dynamic actions of proteins at high altitudes. J. Physiol. U.S.S.R. 31: 349-55; Chem. Abs. 41: 796-7, 1947.

Allan, J. H. 1945. Traumatic calcifications: a precipitating factor in "bends" pain. J. Aviation Med. 16: 235-41.

Allardyce, J., J. Aldous, W. Cooper, J. Pratt and E. Sutherland. 1942. Effects of visible radiations upon albino rats. Am. J. Physiol. 137: 761-8.

Altmann, R. W. and Helmut Schubothe. 1942. Functionelle und organische Schädigungen des zentralnervensystems der Katze im Unterdruckexperiment. (Functional and organic injuries of the central nervous system of cats in low-pressure experiments.) Beitr. path. Anat. 107: 3-116.

Amantea, G. 1933. Sul fattore antineuritico (B₁) e sul concetto di "quoziente beriberico" (QB). (The antineuritic factor (B₁) and the concept of "beriberi quotient" QB.) Atti accad. Lincei 18: 317-23.

(American Society of Heating and Ventilating Engineers.) 1947. Human reaction to atmospheric environment. Heating Ventilating Air Conditioning Guide. 1282 pp.

Amersbach, J. C., L. Nutini and E. S. Cook. 1941. Skin respiration as a dermatologic tool. Arch. Dermatol. Syphilol 43: 949-55.

Andes, E. J. and H. H. Beard. 1934. The effect of inorganic iron with and without ultraviolet irradiation upon the prevention and cure of nutritional anemia. Am. J. Physiol. 108: 91-8.

Armstrong, H. G. 1943. Principles and practices of aviation medicine. Baltimore: Williams and Wilkins Co., 514 pp.

Armstrong, H. G. and J. W. Heim. 1938. The effect of repeated daily exposures to anoxemia. J. Aviation Med. $\underline{9}$: 92-6.

Army Air Forces. 1946. Diet in relation to pilots fatigue. Unpublished manuscript, 5 pp.

Aron, H. C. S., R. M. Craig, C. J. Farmer, H. W. Kendell and G. X. Schwemlein. 1946. Effect of elevated body temperature on plasma vitamin A and carotene. Proc. Soc. Exptl. Biol. Med. $\underline{61}$: 271-6.

Aste-Salazar, H. and A. Hurtado. 1944. The affinity of hemoglobin for oxygen at sea level and at high altitudes. Am. J. Physiol. $\underline{142}$: 733-43.

Bahn, K. 1927. Zur Frage der spezifisch-dynamischen Eiweiss-wirkung und ihres Verhaltens bei Muskelarbeit. (On the question of the specific dynamic effect of protein and the effect upon it of muscular work.) Deut. Arch. Klin. Med. $\underline{156}$: 67-71.

Baicenko, I. P. and A. N. Krestovnikov. 1933a. Über den Zuckergehalt im Blut auf einer Höhe von 4200 m. (The sugar content of the blood at an elevation of 4200 meters.) Arbeitsphysiol. $\underline{6}$: 359-61.

_____ 1933b. Über den Gehalt an Milchsäure im Blut auf einer Höhe von 4200 m. (The lactic acid content of the blood at an altitude of 4200 meters.) Arbeitsphysiol. $\underline{6}$: 373-5.

Baldwin, F. M. and R. J. Shaw. 1938. Relation between B.M.R. and S.D.A. of proteins. Proc. Soc. Exptl. Biol. Med. $\underline{37}$: 705-7.

Barach, A. L. 1937. "Pilot error" and oxygen want with a description of a new oxygen face tent. J. Am. Med. Assoc. $\underline{108}$: 1868-72.

Barach, A. L., M. Eckman, I. Eckman, E. Ginsburg and C. C. Rumsey, Jr. 1947. Studies on positive pressure respiration. III. Effect of continuous pressure breathing on arterial blood gases at high altitude. J. Aviation Med. $\underline{18}$: 139-48.

Barach, A. L., M. Eckman, E. Ginsburg, A. E. Johnson, and R. Brookes. 1946. The effect of ammonium chloride on altitude tolerance. J. Aviation Med. $\underline{17}$: 123-36.

Barach, A. L., M. Eckman, E. Ginsburg, C. C. Rumsey, Jr., Irwin Korr, Irving Eckman and G. Besson. 1946. Studies on positive pressure respiration. I. General aspects and types of pressure breathing. II. Effects on respiration and circulation at sea level. J. Aviation Med. $\underline{17}$: 290-320; 356.

Barach, A. L., W. O. Fenn, E. B. Ferris and C. F. Schmidt. 1947. The physiology of pressure breathing. A brief review of its present status. J. Aviation Med. $\underline{18}$: 73-87.

Barron, E. S. Guzman, D. B. Dill, H. T. Edwards and A. Hurtado. 1937. Acute mountain sickness; the effect of ammonium chloride. J. Clin. Investigation $\underline{16}$: 541-6.

Barcroft, J. 1925. The respiratory function of the blood. Cambridge: Cambridge University Press.

Bateman, J. B. and C. Sheard. 1946. The effect of pressure breathing on the cutaneous temperatures of the extremities. J. Aviation Med. $\underline{17}$: 568-78; 583.

Bean, W. B., L. W. Eichna and W. F. Ashe. 1945. The upper limits of heat and humidity tolerated by acclimatized men working in hot environments. J. Lab. Clin. Med. $\underline{30}$: 357-8.

Behnke, A. R., Jr. 1941-2. Physiologic studies pertaining to deep-sea diving and aviation, especially in relation to the fat content and composition of the body. Harvey Lectures Ser. $\underline{37}$: 198-226.

_____ 1945. The absorption and elimination of gases of the body in relation to its fat and water content. Medicine 24: 359-79.

_____ 1947. Concepts derived from investigations pertaining to high altitude flight. J. Am. Med. Assoc. 133: 450-8.

Behnke, A. R. and T. L. Willmon. 1941. Physiological effects of high altitude. U. S. Navy Med. Bull. 39: 163-78.

Belding, H. S., H. D. Russell, R. C. Darling and G. E. Folk. 1947a. Thermal responses and efficiency of sweating when men are dressed in Arctic clothing and exposed to extreme cold. Am. J. Physiol. 149: 204-22.

_____ 1947b. Analysis of factors concerned in maintaining energy balance for dressed men in extreme cold; effects of activity on the protective value and comfort of an Arctic Uniform. Am. J. Physiol. 149: 223-39.

Benedict, F. G. 1906. The cutaneous excretion of nitrogenous material. J. Biol. Chem. 1: 263-70.

_____ 1938. Vital energetics: A study in comparative basal metabolism. Washington, D. C.: Carnegie Institution of Washington: Publ. No. 503, with 46 illustrations, 215 pp.

Benedict, F. G. and T. M. Carpenter. 1918. Food ingestion and energy transformations with special reference to the stimulating effects of nutrients. Washington, D. C.: Carnegie Institution of Washington: Publ. No. 261, 355 pp.

Benedict, F. G., R. C. Lee and F. Strieck. 1934. The influence of breathing oxygen-rich atmospheres on human respiratory exchange during severe muscular work and recovery from work. Arbeitsphysiol. 8: 266-303.

Benedict, F. G. and G. MacLeod. 1929. The heat production of the albino rat. II. The influence of environmental temperature, age and sex: comparison with the basal metabolism of man. J. Nutrition 1: 367-98.

Benjamin, B., M. Steiner and D. H. Milman. 1948. Value of cytochrome C in anoxia of newborn guinea pigs. Science 107: 142.

Berg, W. E. and S. F. Cook. 1946. Carbon dioxide production of humans at sea level and at low barometric pressures. Am. J. Physiol. 147: 217-21.

Berstein, R. E. 1937. Excretion of vitamin C in sweat. Nature 140: 684-5.

Berry, E. 1915. Über die Abhängigkeit des Stickstoff- und Chlorgehaltes des Schweisses von der Diät. (The relation between the diet, and the nitrogen and chlorine content of the sweat.) Biochem. Z. 72: 285-302.

Bessey, O. A. and O. H. Lowry. 1944. Factors influencing the riboflavin content of the cornea. J. Biol. Chem. 155: 635-43.

Beyne, J., G. Boy, L. Leduc and M. Polonovski. 1945. Elimination urinaire des bases au cours de l'anoxie. (Urinary elimination of bases during anoxia.) Compt. Rend. Soc. Biol. 139: 995-6.

Beyne, J., G. Boy and M. Polonovski. 1944. Phosphates urinaires et hypoxia. (Urinary phosphates and anoxia.) Compt. Rend. Soc. Biol. 138: 174-5.

Bischoff, F., M. L. Long and E. Hill. 1931. Studies in hyperthermia. II. The acid-base equilibrium in hyperthermia induced by short radio waves. J. Biol. Chem. 90: 321-9.

Bischoff, F., L. C. Maxwell and E. Hill. 1931. Studies in hyperthermia. III. The phosphorus equilibrium. J. Biol. Chem. 90: 331-9.

Black, A. and R. W. Swift. 1943. The critical temperature for the albino rat as affected by feeding. J. Nutrition 25: 127-36.

Blair, H. A., R. J. Dern and P. L. Bates. 1947. The measurement of volume of gas in the digestive tract. Am. J. Physiol. 149: 688-707.

Blair, H. A., R. J. Dern and W. O. Fenn. 1943. Abdominal gas. National Research Council, Div. Med. Sci. acting for the Com. Med. Res. O.S.R.D., Com. of Aviation Med., Report No. 193, 11 pp.

Blair, H. A., R. J. Dern and V. G. Smith. 1947. Intestinal gas in simulated flight to high altitude. J. Aviation Med. 18: 352-66.

Blair, J. R., F. W. Urbush and I. T. Reed. 1947. Preliminary observations on physiological, nutritional and psychological problems in extreme cold. Fort Churchill, Canada (Winter, 1946-1947). Section IV. Observations on diet and nutrition. Armored Medical Research Laboratory, Med. Dept. Field Res. Lab., Section IV, July 3, pp. 14-19.

Blasius, W. and E. Bauereisen. 1942. Eine neue Möglichkeit zur Beeinflussung der Höhentoleranz des Menschen in der Unterdruckkammer. (A new possibility of affecting altitude tolerance of human beings in the low-pressure chamber.) Luftfahrtmed. 6: 67.

Block, R. J. and H. H. Mitchell. 1946. The correlation of the amino acid composition of proteins with their nutritive value. Nutrition Abst. and Revs. 16: 249-278.

Blum, H. F. 1941. Photodynamic action and diseases caused by light. New York: Reinhold Publishing Corporation, 309 pp.

_____ 1943. Military aspects of sunburn. War Medicine 4: 388-99.

_____ 1945a. The physiological effects of sunlight on man. Physiol. Rev. 25: 483-530.

_____ 1945b. The solar heat load: its relationship to total heat load and its relative importance in the design of clothing. J. Clin. Investigation 24: 712-21.

Blum, H. F., M. Eicher and W. S. Terus. 1946. Evaluation of protective measures against sunburn. Am. J. Physiol. 146: 118-25.

Bock, A. V. 1944. Physiological adaptations of man to heat; rations; field methods and kits. OEMcmr-328, Bimonthly Progress Report No. 6 to Com. Med. Res., O.S.R.D., November 1, p. 1.

Bogue, J. Y., C. L. Evans and R. A. Gregory. 1939. The effect of adrenaline, together with acute anoxia on the heart glycogen. Quarterly J. Exptl. Physiol. 29: 83-90.

Booher, L. E. and E. C. Callison. 1939. The minimum vitamin-A requirements of normal adults. II. The utilization of carotene as affected by certain dietary factors and variations in light exposure. J. Nutrition 18: 459-71.

Booth, G. and J. M. Strang. 1936. Changes in temperature of the skin following the ingestion of food. Arch. Intern. Med. 57: 533-43.

Boothby, W. M., W. R. Lovelace, II and O. O. Benson. 1940. High altitude and its effect on the human body. I. J. Aeronautical Sci. 7: 461-8.

Borchardt, W. 1930. Die Magenfunktion im Kunstlichen Tropenklima. (Gastric function in an artificial tropical climate.) Klin. Wochschr. 9: 886-8.

_____ 1931. Aufgaben der Tropenphysiologie. (Problems of the physiology of the tropics.) Ergeb. d. Physiol. 31: 96-131.

Bordet, F., M. Brongniart and J. Volckringer. 1941. The possible role of ergot substances in the vascular disturbances of the extremities after freezing. Bull. Acad. Med. 125: 377-9; Chem. Abs. 37: 5481, 1943.

Borgstrom, P. and R. W. Bost. 1926-7. Study of the protein intake as indicated by urinary nitrogen. Am. J. Physiol. 79: 229-36.

Bornstein, A. and A. Loewy. 1931. Über den Alkoholumsatzbeim Menschen im Höhenklima. (The metabolism of alcohol by man at high altitudes.) Biochem. Z. 230: 51-67.

Bost, R. W. and P. Borgstrom. 1926-27. Cutaneous excretion of nitrogenous material in New Orleans. Am. J. Physiol. 79: 242-4

Boy, G. and J. Cheymol. 1946. Etude des échanges respiratoires en altitude chez le Lapin à différents ages. (Respiratory exchanges at high altitudes in rabbits of different ages.) Bull. Soc. Chim. Biol. 28: 382-9.

Britton, S. W. 1928. Studies of the conditions of activity in endocrine glands. XXII. Adrenin secretion on exposure to cold, together with a possible explanation of hibernation. Am. J. Physiol. 84: 119-131.

Britton, S. W. and R. F. Kline. 1945. Age, sex, carbohydrate, adrenal cortex and other factors in anoxia. Am. J. Physiol. 145: 190-202.

Britton, S. W., V. A. Pertzoff, C. R. French and R. F. Kline. 1947. Circulatory and cerebral changes and protective aids during exposure to acceleratory forces. Am. J. Physiol. 150: 7-26.

Brody, S. 1927. Growth rates during the self-inhibiting phase of growth. Missouri Agr. Exp. Sta. Res. Bull. 101: 26 pp.

Bronshtein, Y. E. 1944. The effect of hypoxemia on secondary C-hypovitaminosis. Am. Rev. Soviet Med. 1: 314-16.

Brooks, M. M. 1945. The effect of methylene blue on performance efficiency of high altitudes. J. Aviation Med. 16: 250-62.

Brown, A. H. and E. J. Towbin. 1944. Circulatory strains of heat, work and dehydration. Concerning water metabolism in desert troops. OEMcmr-206, Interim Report No. 17 to Com. Med. Res., O.S.R.D. June 1, 12 pp.

Brown, B. R. 1946. The incidence and relation of syncope to decompression sickness. J. Aviation Med. 17: 257-64.

Brown, G. A., C. H. Cronick, H. J. Motley, E. J. Kokour and W. O. Klingman. 1944. Nervous system dysfunction during and following oxygen-controlled, high-altitude indoctrination. Trans. Am. Neurol. Assoc. 70: 113-17.

Brown, W. H. and J. F. McCreary. 1943. Field test trials of rations, Camp Penobsquis, N. B., September 2-11, 1942. Ottawa, Canada, Edmond Cloutier.

Brunquist, E. H., E. J. Schneller and A. S. Loevenhart. 1924. The effects of anoxemia on nitrogen metabolism. J. Biol. Chem. 62: 93-115.

Bryan, A. H. and H. T. Ricketts. 1944. The effect in man of chronic intermittent anoxia on glucose tolerance and the urinary excretion of sodium, potassium, chloride, phosphorus, nitrogen and 17-ketosteroids. Endocrinology 35: 215-6P.

Bryant, J. E. and G. A. Talbert. 1931. Calcium as a normal constituent of the sweat. Proc. Am. Physiol. Soc., Am. J. Physiol. 97: 509.

Burkhardt, W. L., H. F. Adler, A. F. Thometz, A. J. Atkinson and A. C. Ivy. 1947. Decompression sickness. Some factors which affect the incidence of bends at altitude. J. Am. Med. Assoc. 133: 373-7.

Burrill, Marie W., S. Freeman and A. C. Ivy. 1945. Sodium, potassium and chloride excretion of human subjects exposed to a simulated altitude of eighteen thousand feet. J. Biol. Chem. 157: 297-302.

Burtenshaw, J. M. L. 1942. The mechanism of self-disinfection of the human skin and its appendages. J. Hygiene 42: 184-210.

Burton, A. C. and D. W. Bronk. 1937. The motor mechanism of shivering and of thermal muscular tone. Am. J. Physiol. 119: 284P.

Burton, A. C. and J. R. Murlin. 1935. Human calorimetry. III. Temperature distribution, blood flow and heat storage in the body in basal condition and after ingestion of food. J. Nutrition 9: 281-300.

Burton, A. C., J. C. Scott, B. McGlone and H. C. Bazett. 1940. Slow adaptation in the heat exchanges of man to changed climatic conditions. Am. J. Physiol. 129: 84-101.

Büsing, K. H. and W. Kauff. 1942. Untersuchungen über den Kreatinhaushalt unter den Bedingungen des Höhenfluges und seine Beeinflussbarkeit durch Vitamin B₁. (The creatine balance during flying at high altitude and the effect of vitamin B₁.) Hoppe-Seyler's Z. physiol. Chem. 276: 87-96.

Camis, M. 1936. Metabolismo basale ed alimentazione in Somalia. Primo contributo alla fisiologia tropicale in Africa orientale. (Basal metabolism and diet in Italian Somaliland. First contribution to tropical physiology in East Africa.) R. Accad. Italia. Centro. Studi per l' Africa Orientale Italiana Rome,110 pp.; Nutrition Abs. and Revs. 7: 105, 1937.

Campbell, J. A. 1938. Increase of resistance to oxygen want in animals on certain diets. Quart. J. Exptl. Physiol. 28: 231-41.

_____ 1939. Diet and resistance to oxygen want ׀ Quart. J. Exptl. Physiol. 29: 259-75.

Capstick, J. W. and T. B. Wood. 1922. The effect of change of temperature on the basal metabolism of swine. J. Agr. Sci. 12: 257-268.

Carpenter, R. and G. A. Talbert. 1932. Magnesium secreted in the sweat and its relation to the calcium content. Proc. Am. Physiol. Soc., Am. J. Physiol. 101: 17-18.

Caspari, W. and C. Schilling. 1920. Über den Stoffwechsel der Europäer in den Tropen. (The metabolism of the European in the tropics.) Z. Hygiene Infektionskrankh. 91: 57-132.

Catchpole, H. R. and I. Gersh. 1946. Bubble formation in rabbits decompressed to altitude: effect of preoxygenation, electrical stimulation, and some pharmacological factors. J. Cell. and Comp. Physiol. 27: 27-34.

_____ 1947. Pathogenetic factors and pathological consequences of decompression sickness. Physiological Reviews 27: 360-97.

Chambers, A. H., G. Brewer, H. W. Davenport and S. Goldschmidt. 1947. The respiratory responses to anoxemia of the normal unanesthetized dog and their causes. Am. J. Physiol. 148: 392-405.

Champy, C. and R. Coujard. 1940. Localisation et acceleration par le froid des nevrites de l'avitaminose B₁. (Localisation and acceleration by cold of the neuritis from vitamin B₁ deficiency.) Compt. Rend. Acad. Sci. 210: 150-2.

Charipper, H. A., E. D. Goldsmith and A. S. Gordon. 1945. Vitamin deficiency and overdosage and the resistance of rats to lowered barometric pressures. Am. J. Physiol. 145: 130-33.

Chatron, M. 1933. Sur las composition chimique de la sueve recueillie dans les etuves romaines de Plombières-les-Bains. (The chemical composition of the sweat collected in the Romal baths at Plombières-les Bains.) Bull. Soc. Chim. Biol. 15: 1107-12.

Chick, H. and E. M. Hume. 1920. The production in monkeys of symptoms closely resembling those of pellagra, by prolonged feeding on a diet of low protein content. Biochem. J. 14: 135-46.

Christensen, E. H. 1933. Beiträge zur Physiologie schwerer körperlicher Arbeit. IX. Mitteilung: Hyperthermie und Ruhestoffwechsel. (The physiology of severe muscular work. IX. Hyperthermy and rest metabolism.) Arbeitsphysiol. 7: 120-6.

_____ 1937. Sauerstoffaufnahme und respiratorische Funktionen in grossen Höhen. (Oxygen uptake and respiratory functions at great heights.) Skand. Arch. Physiol. 76: 88-100.

_____ 1945. Droppslig aktivitet pa stora höjder. (Muscular work at high altitudes.) Nord. Med. 27: 1956-1960; Nutrition Abs. Rev. 16: 876, 1947.

Christensen, E. H. and H. Smith. 1936. Fliegeruntersuchungen. 3. Mitt.: Die Wirkung von Ammoniumchlorid auf Höhenflieger. (Aviation experiments. 3. The effect of ammonium chloride on the aviator.) Skand. Arch. Physiol. 73: 155-8.

Christensen, W. R. 1947. Long term acclimatization to heat. Am. J. Physiol. 148: 86-90.

Christensen, W. R. and M. Clinton, Jr. 1947. Effect of cytochrome C therapy on altitude tolerance of normal rats. Proc. Soc. Exptl. Biol. Med. 66: 360-1.

Clark, W. G. and H. Jorgenson. 1945a. Effect of ingestion of fluid and food on G tolerance. OEMcmr-288, Com. on Aviation Med. Report No. 490 to O.S.R.D., November 9, 4 pp.

_____ 1945b. Effect of ingestion of food on tolerance of human subjects to positive acceleration. National Research Council, Div. Med. Sci. acting for Com. Med. Res., O.S.R.D., Com. Aviation Med., Abstract of Report No. 502, December 30.

Clark, W. G., I. D. R. Gordiner, A. K. McIntyre and H. Jorgenson. 1945. Effect of hyperglycemia and insulin on G tolerance. National Research Council, Div. Med. Sci., acting for Com. Med. Res., O.S.R.D., Com. Aviation Med., Report No. 486, October 29, 3 pp.

Clarke, R. W., C. Marshall and L. F. Nims. 1944. Blood pH during decompression. Am. J. Physiol. 142: 483-6.

Clinton, M., Jr., G. W. Thorn and V. D. Davenport. 1946. Studies on altitude tolerance. 2. Studies on normal human subjects--effect of repeated short exposure to reduced atmospheric pressure. Bull. Johns Hopkins Hospital 79: 70-89.

Cluver, E. H. 1932. An analysis of ninety-two fatal heat stroke cases in the Witwatersrand gold mines. So. African Med. J. 6: 19-22.

Cohn, H. and H. Gessler. 1925. Untersuchungen über die Wärmeregulation. IV. Mitteilung. Warmeregulation und Eiweissumsatz. (Studies on the heat regulation. IV. Heat regulation and protein metabolism.) Pflüger's Arch. ges. Physiol. 207: 396-401.

Conn, J. W. and E. S. Conn. 1941. Metabolism in organic hyper-insulinism. III. Effects of adrenal cortical extract on blood sugar and on sodium and nitrogen equilibrium. Arch. Intern. Med. 68: 1115-9.

Conn, J. W. and M. W. Johnston. 1944. Improvement of ability of soldier to work in humid heat. Salt requirements of acclimatized men performing hard work in a tropical climate. OEMcmr-232 Report No. 10 to the Com. Med. Res., O.S.R.D., July 1, p. 1.

1945. Improvement of ability of soldier to work in humid heat. OEMcmr-232, Monthly Progress Report No. 15, Com. Med. Res., O.S.R.D., May, 2 pp.

Conn, J. W., M. W. Johnston and L. H. Louis. 1946. Relationship between salt intake and sweat salt concentration under conditions of hard work in humid heat. Federation Proc. 5: 230.

Consolazio, F. C. and W. H. Forbes. 1946. The effects of a high fat diet in a temperate environment. J. Nutrition 32: 195-211.

Consolazio, W. V., M. B. Fisher, N. Pace, L. J. Pecora, G. C. Pitts and A. R. Behnke. 1947. Effects on man of high concentrations of carbon dioxide in relation to various oxygen pressures during exposures as long as 72 hours. Am. J. Physiol. 151: 479-503.

Consolazio, W. V., L. J. Pecora and T. Tusing. 1947. A slow dissolving, nonirritating salt tablet for use in hot environments. J. Indust. Hygiene Toxicol. 29: 347-50.

Cook, S. F. 1945. The inhibition of animal metabolism under decompression. J. Aviation Med. 16: 268-271.

Cook, S. F. and E. Strajman. 1945. The effect of decompression on human metabolism during and after exercise. Am. J. Physiol. 144: 637-42.

Corcoran, A. C. and I. M. Rabinowitch. 1937. A study of the blood lipoids and blood protein in Canadian Eastern Arctic Eskimos. Biochem. J. 31: 343-348.

Corey, E. L. 1947. An experimental study of explosive decompression injury. Am. J. Physiol. 150: 607-12.

Cornbleet, Theodore. 1933. Self-sterilizing powers of the skin. V. Are they endowed by the surface acid? Arch. Dermatol. Syphilol. 28: 526-31.

Cornbleet, T., E. R. Kirch and O. Bergeim. 1943. Excretion of thiamine, riboflavin, niacin and pantothenic acid in human sweat. J. Am. Med. Assoc. 122: 426-9.

Cornbleet, T., R. I. Klein and E. R. Pace. 1936. Vitamin content of sweat. Arch. Dermatol. Syphilol. 34: 253-4.

Cowgill, G. R. and D. L. Drabkin. 1927. Determination of a formula for the surface area of the dog together with a consideration of formulae available for other species. Am. J. Physiol. 81: 36-61.

Craig, F. N. 1943. The effect of anoxia on the metabolism of liver slices from fed and fasted rats. J. Biol. Chem. 150: 209-12.

Craig, R. M., G. X. Schwemlein, H. W. Kendall, C. J. Farmer and H. C. S. Aron. 1946. Effect of elevated body temperature on the plasma ascorbic acid. Arch. Phys. Med. 27: 603-7.

Crew, W. H. and C. H. Whittle. 1938. On the absorption of ultraviolet radiation by human sweat. J. Physiol. 93: 335-48.

Crile, G. W. and D. P. Quiring. 1939. Indian and Eskimo metabolism. J. Nutrition 18: 361-8.

Crocker, E. C. 1945. Flavor. New York: McGraw-Hill Book Company, Inc., 172 pp.

Crowley, L. V., R. E. Johnson and G. V. Anderson. 1947. Medical nutritional aspects of troops allowed free choice of any quantity of any item in a packaged ration. Federation Proc. 6: 404-5.

Cuthbertson, D. P. and W. S. W. Guthrie. 1934. The effect of variations in protein and salt intake on the nitrogen and chloride content of sweat. Biochem. J. 28: 1444-53.

Daly, C. and D. B. Dill. 1937. Salt economy in humid heat. Am. J. Physiol. 118: 285-9.

D'Angelo, S. A. 1946a. Urinary output and phosphorus excretion in human subjects during prolonged exposures at low simulated altitudes. Proc. Soc. Exptl. Biol. Med. 62: 13-7.

_____ 1946b. Blood sugar levels and carbohydrate administration in human subjects during prolonged exposures to moderately low altitudes. Am. J. Physiol. 145: 365-75.

_____ 1946c. The respiratory metabolism of human subjects during prolonged exposures to simulated altitudes of 8000 and 10,000 feet. Am. J. Physiol. 146: 710-22.

Danielson, W. H., R. M. Stecher, E. Muntwyler and V. C. Myers. 1938. The acid-base balance of the blood serum in hyperthermia. Am. J. Physiol. 123: 550-7.

Daum, K., K. Boyd and W. D. Paul. 1939. Influence of fever therapy on blood levels and urinary excretion of ascorbic acid. Proc. Soc. Exptl. Biol. Med. 40: 129-32.

Dawbarn, M. C. 1924. Negative result of an attempt to sensitize white mice to the action of ultra-violet light by a diet deficient in tryptophan. Australian J. Exptl. Biol. Med. Sci. 1: 73-5.

De Michele, G. and G. Scoz. 1944. Action of acetylcholine on maximum tolerance to oxygen deficiency and on the erythrocyte count. Boll. Soc. Ital. Biol. Sper. 19: 6-7; Chem. Abs. 41: 1754, 1947.

De Moura Campos, F. A. 1937. Basal metabolism in tropical and sub-tropical countries. Proc. Royal Acad. of Italy, pp. 68-92.

Denhoff, E. 1945. Hematologic values of American soldiers stationed in the tropics. J. Lab. Clin. Med. 30: 874-82.

Denis, W. and P. Borgstrom. 1924. A study of the effect of temperature on protein intake. J. Biol. Chem. 61: 109-16.

Dietrich, S. and E. Pendl. 1937. Vitamin B_2 (Lactoflavin) und Erstickung des isoleirten Froschherzens. (Vitamin B_2 (lactoflavin) and anoxia of the isolated frog heart.) Klin. Wochenschr. 16: 13-5.

Dill, D. B. 1947. Food preferences on combat flights. J. Aviation Med. 18: 590-3.

Dill, D. B., F. G. Hall and H. T. Edwards. 1938. Changes in composition of sweat during acclimatization to heat. Am. J. Physiol. 123: 412-19.

Dill, D. B., R. E. Johnson and R. M. Kark. 1946. Feeding problems in man as related to environment. QMC, W44-109-qm-986. Annual Report, June 30, 126 pp.

Dill, D. B., B. F. Jones, H. T. Edwards and S. A. Oberg. 1933. Salt economy in extreme dry heat. J. Biol. Chem. 100: 755-67.

Di Macco, G. 1945. Calcium and hypoxia. Boll. Soc. Ital. Biol. Sper. 20: 520-1; Chem. Abs. 40: 6663, 1946.

Dixon, K. C. 1940. A study of cortical metabolism in relation to cerebral disease. Brain 63: 191-9.

Dobbelstein, O. 1940. Experimentelle Untersuchungen zur Frage des erhohten C-Vitamin-verbrauches bei Fieber. (Experimental investigations of increased vitamin C consumption during fever.) Z. ges. exptl. Med. 107: 532-6.

Dohan, F. C. 1942. Effect of low atmospheric pressure on the adrenals, thymus and testes of rats. Proc. Soc. Exptl. Biol. Med. 49: 404-8.

Donhoffer, S. and J. Vonotzky. 1947a. The effect of environmental temperature on food selection. Am. J. Physiol. 150: 329-33.

————. 1947b. The effect of thyroxine on food intake and selection. Am. J. Physiol. 150: 334-9.

Dorfman, R. I., B. N. Horwitt and W. R. Fish. 1942. The presence of a cortin-like substance (cold protecting material) in the urine of normal men. Science 96: 496-7.

Dorfman, R. I., R. A. Shipley, E. Ross, S. Schiller and B. N. Horwitt. 1946. The relative potencies of adrenal cortical steroids as determined by a cold-protection test and by a glycogen-deposition test. Endocrinology 38: 189-96.

Dorrance, S. S., G. W. Thorn, M. Clinton, Jr., H. W. Edmonds and S. Farber. 1943. Effect of cobalt on work performance under conditions of anoxia. Am. J. Physiol. 139: 399-405.

Dorrance, S. S., G. W. Thorn, F. H. Tyler and B. Katzin. 1942. Work performance of normal rats under conditions of anoxia. Endocrinology 31: 209-16.

Douglas, C. G., C. R. Greene and F. G. Kergin. 1933. The influence of ammonium chloride on adaptation to low barometric pressures. J. Physiol. 78: 404-14.

Dove, W. F. 1946. Developing food acceptance research. Science 103: 187-190.

Drabkin, D. L. 1947. Liver regeneration and cytochrome c metabolism. Influence of anoxia and of injection of cytochrome c. J. Biol. Chem. 171: 409-17.

Dreosti, A. O. 1935-6. Problems arising out of temperature and humidity in deep mining on the Witwatersrand. The results of some investigations into the medical aspect of deep mining on the Witwatersrand. J. Chem. Met. and Mining Soc. of S. Africa 36: 102-129.

Drinker, C. K. 1936. The effects of heat and humidity upon the human body. J. Indust. Hygiene Toxicol. 18: 471-85.

Dripps, R. D. and J. H. Comroe, Jr. 1947. The effect of the inhalation of high and low oxygen concentrations on respiration, pulse rate, ballistocardiogram and arterial oxygen saturation (oximeter) of normal individuals. Am. J. Physiol. 149: 277-91.

Droese, W. 1942. Die Wirkung von Traubenzucker und Traubenzucker B_1-Kombinationen auf die Leistungsfähigkeit bei Hitzearbeit. (The effect of glucose and glucose-vitamin B_1 combinations on the capacity for work at high temperatures.) Arbeitsphysiologie 12: 124-33.

DuBois, E. F. 1936. Basal metabolism in health and disease. Philadelphia: Lea and Febinger. 3rd edition. 494 pp.

Dugal, L.-P. 1944. Resistance to extreme temperatures in connection with different diets. Proc. Fourteenth Meeting Associative Com. Med. Res., National Research Council, Canada C1029 September, 2 pp.

Dugal, L.-P. and M. Thérien. 1947. Ascorbic acid and acclimatization to cold environment. Canadian J. Res. 25 E: 111-36.

Duguet, J., P. Dumont and J.-P. Bailliart. 1947. The effects of anoxia on retinal vessels and retinal arterial pressure. J. Aviation Med. 18: 516-20.

Eberhard, H. M. 1940. Temperature of the gastrointestinal tract and the effect thereon of hot and cold drinks and of physical therapeutic agents. Rev. Gastroenterol. 7: 133-4.

Eckman, M., et al. 1945. Oxygen consumption under basal conditions at sea level and at altitude. OEMcmr-47, Com. Aviation Med. Report No. 445, June 20.

Eckman, M., B. Barach, C. A. Fox, C. C. Rumsey, Jr. and A. L. Barach. 1945. Effect of diet on altitude tolerance. J. Aviation Med. 16: 328-41.

Eckman, M., B. Barach, C. Fox, C. C. Rumsey, Jr., E. Somkin and A. L. Barach. 1947. An appraisal of intermittent pressure breathing as a method of increasing altitude tolerance. J. Aviation Med. 18: 565-74.

Edelmann, A., W. V. Whitehorn, A. Lein and F. A. Hitchcock. 1946. Pathological lesions produced by explosive decompression. J. Aviation Med. 17: 596-601; 612.

Edison, A. O., R. H. Silber and D. M. Tennent. 1945. The effect of varied thiamine intake on the growth of rats in tropical environment. Am. J. Physiol. 144: 643-51.

(Editorial) 1940. Diet, oxygen want and high flying. British Med. J. i: 57-8.

Edwards, E. A. and S. Q. Duntley. 1939. The pigments and color of living human skin. Am. J. Anat. 65: 1-33.

Edwards, H. T. 1936. Lactic acid in rest and work at high altitude. Am. J. Physiol. 116: 367-75.

Ehrismann, O. 1938. The metabolism of men working under different climatic conditions. Z. Hygiene Infektionskrankh. 120: 319-40; Chem. Abs. 32: 6706, 1938.

Eichna, L. W., W. F. Ashe, W. B. Bean and W. B. Shelley. 1945. The upper limits of environmental heat and humidity tolerated by acclimatized men working in hot environments. J. Indust. Hygiene and Toxicol. 27: 59-84.

Engel, G. L., J. P. Webb and E. B. Ferris. 1945. Quantitative electroencephalographic studies of anoxia in humans; comparison with acute alcoholic intoxication and hypoglycemia. J. Clin. Investigation 24: 691-7.

Eppright, E. S. 1947. Factors influencing food acceptance. J. Am. Dietetic Assoc. 23: 579-87.

Evans, G. 1934. The effect of low atmospheric pressure on the glycogen content of the rat. Am. J. Physiol. 110: 273-7.

Falconer, M. A. and A. Lyall. 1937. The requirements of sodium chloride. British Med. J. ii: 1116-1118.

Falke. 1939. Über die Grösse des Vitamin C. Verbrauchs im Fieber. (Vitamin C requirement in fever.) Klin. Wochenschr. 18: 818-821.

Fazekas, J. F. and H. E. Himwich. 1943. Anaerobic survival of adult animals. Am. J. Physiol. 139: 366-70.

von Fellenberg, T. 1926. Das Vorkommen, der Kreislauf und der Stoffwechsel des Jods. IV. Untersuchungen über den Jodstoffwechsel. (The occurrence, circulation and metabolism of iodine. IV. Iodine metabolism.) Ergebnisse Physiol. 25: 298-330.

Fenn, W. O. 1944. Effects of anoxia and acapnia on performance. OEMcmr-147, Prog. Report No. 18 to Com. Med. Res., O.S.R.D., December 1.

Fenn, W. O., H. Rahn and A. B. Otis. 1946. A theoretical study of the composition of the alveolar air at altitude. Am. J. Physiol. 146: 637-53.

Ferraloro, G. 1929. Ricerche sul ricambo degli idrati di carbonio in alta montagna. (Studies on carbohydrate metabolism on a high mountain.) Arch. Sci. Biol. 13: 109-26; Chem. Abs. 23: 3260, 1929.

Ferrero, S. 1940. Action of nicotinic acid in passive hyperthermia. Riv. Patol. Sper. 24: 259-78; Chem. Zentr. 1941, II, 2222.

Filippovich, S. I. 1940. Changes of salivation under the influence of reduced barometric pressure. Bull. Biol. Med. Exptl. U.S. S. R.: 338-40 (in English).

Finney, W. H., S. Dworkin and G. J. Cassidy. 1927. The effects of lowered body temperature and of insulin on the respiratory quotients of dogs. Am. J. Physiol. 80: 301-310.

Fishberg, E. H. and W. Bierman. 1932a. Acid-base balance in sweat. J. Biol. Chem. 97: 433-41.

_____ 1932b. Excretion of lactic acid in sweat. Proc. Soc. Exptl. Biol. Med. 29: 1021-2.

Foltz, E. E. and A. C. Ivy. 1943. Effect of simulated high altitudes on subsequent work output. War Medicine 4: 471-4.

Forbes, W. H. 1936. Blood sugar and glucose tolerance at high altitudes. Am. J. Physiol. 116: 309-16.

Forster. 1940. Die Steigerung der Höhenfestigkeit durch Kreislaufmittel und Vitamine. (The increase in resistance to altitude through way of circulation and vitamins.) Marburg. Inaug.-diss. (quoted by Büsing and Kauff, Hoppe-Seyler's Z. Physiol. Chem. 276: 87-96, 1942).

Foster, P. C. 1931. The effects of radiant energy on milk anemia in rats. J. Nutrition 4: 517-24.

_____ 1935. Effect of infra-red on tissue temperature gradient as influenced by pigment. Proc. Soc. Exptl. Biol. Med. 33: 62-64.

Foulger, J. H. 1942. Vitamin C prevents heat cramps and heat prostration. Science 95: No. 2477, Suppl., p. 12.

Fourt, L. and M. Harris. 1944. Wind effect on evaporation through fabrics. OEMcmr-304, Progress Report No. 9 to Com. Med. Res. to O.S.R.D., August 1. Taken from Sum. of Repts. to C.M.R. of O.S.R.D., July 31 to August 5, 1944; Bull. 1, August 7, 1944.

Fox, F. W. 1940. Ascorbic acid (vitamin C) and human nutrition. A critical review of the more recent literature. Proc. Transvaal Mine Med. Officers' Assoc. 19: 249-66.

Fox, F. W. and L. F. Dangerfield. 1940. Scurvy and the requirements of native mine labourers for the anti-scorbutic vitamin. An experimental study. Proc. Transvaal Mine Med. Officers' Assoc. 19: 267-88.

Frazier, R. G. 1945. Acclimatization and the effects of cold on the human body as observed at little America III, on the United States Antarctic Service Expedition 1939-1941. Proc. Am. Philos. Soc. 89: 249-55.

Freeman, W., G. Pincus and E. D. Glover. 1944. The excretion of neutral urinary steroids in stress. Endocrinology 35: 215P.

Freyberg, R. H. and R. L. Grant. 1937. Loss of minerals through the skin of normal humans when sweating is avoided. J. Clin. Investigation 16: 729-31.

Friedemann, T. E. Effects of a high carbohydrate diet in raising the ceiling of men under the condition of anoxia (SPQRD 430, low protein). V. A review of the literature on relation of tolerance to high altitude to the effect of diet, with special reference to carbohydrate; also theoretical considerations. Report to B. E. Proctor, Special Assistant, War Department, Office of the Quartermaster General (undated) pp. 4-20.

Friedemann, T. E., G. E. Haugen and T. C. Kmieciak. 1945. Pyruvic acid. III. The level of pyruvic and lactic acids and the lactic-pyruvic ratio in the blood of human subjects. The effect of food, light muscular activity, and anoxia at high altitude. J. Biol. Chem. 157: 673-89.

Friedemann, T. E. and A. C. Ivy. 1947. Work at high altitude. I. Plan of study and methods. Quart. Bull. Northwestern University Med. School 21: 31-44.

Friedman, Nathan B. 1946. The reactions of tissue to cold. The pathology of frostbite, high-altitude frostbite, trench foot and immersion foot. Am. J. Clin. Path. 16: 634-9.

Fuhrman, F. A. and J. M. Crismon. 1947. The influence of acute hypothermia on the rate of oxygen consumption and glycogen content of the liver and of the blood glucose. Am. J. Physiol. 149: 552-60.

Fuhrman, F. A., G. J. Fuhrman and J. Field, 2nd. 1945. Oxygen consumption of excised rat tissues following acute anoxic anoxia. Am. J. Physiol. 144: 87-90.

Gagge, A. P., S. C. Allen and J. P. Marbarger. 1945. Pressure breathing. J. Aviation Med. 16: 2-8.

Gagge, A. P., A. C. Burton and H. C. Bazett. 1941. A practical system of units for the description of the heat exchange of man with his environment. Science 94: 428-30.

Galvão, P. E. 1947. Heat production in relation to body weight and body surface. Inapplicability of the surface law on dogs of the tropical zone. Am. J. Physiol. 148: 478-89.

Garasenko, V. M. 1944. The use of carbon dioxide at lowered barometric pressures. Am. Rev. Soviet Med. 2: 119-25.

Gardner, T. S. and F. B. Forbes. 1945. The effect of thiourea on mice undergoing an abrupt reduction of external atmospheric pressure. J. Aviation Med. 16: 99-100.

Gellhorn, E. 1937. Oxygen deficiency, carbon dioxide and temperature regulation. Am. J. Physiol. 120: 190-4.

Gellhorn, E. and H. Hailman. 1943. The effect of anoxia on sense organs. Federation Proc. 2: 122-6.

Gellhorn, E. and H. Hailman. 1944. The parallelism in changes of sensory function and electroencephalogram in anoxia and the effect of hypercapnia under these conditions. Psychosom. Med. 6: 23-30.

Gellhorn, E. and A. C. Packer. 1939. Influence of anoxia on glycogenolytic action of adrenalin. Proc. Soc. Exptl. Biol. Med. 41: 345-6.

————— 1940. Studies on the interaction of hypoglycemia and anoxia. Am. J. Physiol. 129: 610-17.

Gemmill, C. L. 1941. Acclimatization to high altitudes. A review of physiological observations. U. S. Naval Med. Bull. 39: 178-87.

————— 1943. Physiology in aviation. Springfield, Illinois and Baltimore: Charles C. Thomas, 129 pp.

————— 1946. Aviation physiology. Ann. Revs. Physiol. 8: 499-514.

Geppert, M. P., A. Peña and H. Schaefer. 1944. Der Einfluss von Calcium und Yohimbin auf die Höhenfestigkeit. (The influence of Ca and yohimbine on resistance to altitude.) Luftfahrtmed. 8: 357-67.

87

Gerking, S. D. and S. Robinson. 1946. Decline in the rates of sweating of men working in severe heat. Am. J. Physiol. 147: 370-8.

Gershon-Cohen, J., H. Shay and S. S. Fels. 1940. The relation of meal temperature to gastric motility and secretion. Am. J. Roentgen. Radium Therapy 43: 237-42.

Giaja, J. 1925. Le métabolisme de sommet et le quotient métabolique. (Summit metabolism and metabolic quotient.) Ann. Physiol. et Physico-chim. Biol. 1: 596-627.

_____ 1932. Influence de la fatigue musculaire sur la puissance thermogénétique et la resistance au froid. (Effect of muscular fatigue on heat regulating power and resistance to cold.) Ann. Physiol. et Physico-chim. Biol. 8: 535-45.

_____ 1938. La dépression barométrique et l'action dynamique spécifique des protides. (Effect of decrease in atmospheric pressure on the specific dynamic action of proteins.) Compt. Rend. Soc. Biol. 128: 687-8.

Giaja, J. and S. Gelineo. 1934. Alimentation et résistance au froid. (Diet and resistance to cold.) Compt. Rend. Acad. Sci. 198: 2277-8.

Gibbs, F. A., E. L. Gibbs, W. G. Lennox and L. F. Nims. 1943. The value of CO_2 in counteracting the effects of low O. J. Aviation Med. 14: 250-61.

Giragossintz, G. and E. S. Sundstroem. 1937. Cortico-adrenal insufficiency in rats under reduced pressure. Proc. Soc. Exptl. Biol. Med. 36: 432-4.

Glickman, N. and E. Gellhorn. 1938. The effect of oxygen deficiency on the sensitivity of rats to insulin. Am. J. Physiol. 121: 358-63.

Glickman, N., R. W. Keeton, H. H. Mitchell and M. K. Fahnestock. 1946. The tolerance of man to cold as affected by dietary modifications: high versus low intake of certain water-soluble vitamins. Am. J. Physiol. 146: 538-58.

Glickman, N., H. H. Mitchell, E. H. Lambert and R. W. Keeton. The total specific dynamic action of high-protein and high-carbohydrate diets on human subjects. J. Nutrition (in press).

Goebel, F. and S. Marczewski. 1938. Acclimatization of the human organism to low atmospheric pressure. Acta Biol. Exptl. (Warsaw) 12: 87-9; Chem. Abs. 33: 6409, 1939.

Goetzl, F. R. and F. Stone. 1946. Human appetite. QMC-W11-009-qm-70134 Report No. 1, October 1, p. 1.

Gold, E. 1935. The effect of wind, temperature, humidity and sunshine on the loss of heat of a body at temperature 98° F. Quart. J. Roy. Meterol. Soc. 61: 316-31.

Goralewski, G. 1937. Der Einfluss von Sauerstoffmangel auf den Calciumspiegel im Blut. (The influence of low oxygen on blood calcium.) Luftfahrtmed. 1: 338-43.

Gordon, A. S. and M. Dubin. 1934. On the alleged presence of "hemopoietine" in the blood serum of rabbits either rendered anemic or subjected to low pressures. Am. J. Physiol. 107: 704-8.

Gordon, A. S., E. D. Goldsmith, and H. A. Charipper. 1944. Thiourea and resistance to low atmospheric pressure ("high altitudes"). Science 99: 104-5.

Gordon, A. S., E. D. Goldsmith, and H. A. Charipper. 1945. Effects of p-aminobenzoic acid and thiouracil on thyroid function and resistance to low pressures. Endocrinology 37: 223-9.

Gordon, A. S. and W. Kleinberg. 1937. Red cell and reticulocyte counts in guinea pigs following exposure to low pressures. Proc. Soc. Exptl. Biol. Med. 37: 507-9.

Gorelov, I. I. 1939. Changes in the mineral content of the blood under conditions of reduced atmospheric pressure. J. Physiol. (U.S.S.R.) 27: 490-8 (in English, 498).

Govier, W. M. 1944. Rationale for use of vitamins in the therapy of shock and anoxia. J. Am. Med. Assoc. 126: 749-50.

Govier, W. M. and C. M. Greer. 1941. Studies on shock induced by hemorrhage. II. Effect of thiamine on disturbances of carbohydrate metabolism. J. Pharmocol. Exptl. Therap. 72: 321-30.

Govier, W. M. and M. E. Greig. 1943. Studies on shock induced by hemorrhage. V. The effect of cellular damage on the in vitro hydrolysis and synthesis of cocarboxylase by liver tissue. J. Pharmacol. Exptl. Therap. 79: 240-5.

Grab, W. and K. Lang. 1944. Kälteresistenz und Ernährung. 2. Einfluss der Zufuhr der Vitamine A und B auf de Kälteresistenz. (Cold resistance and nutrition. 2. Effect of addition of vitamins A and B on cold resistance.) Klin. Wochenschr. 21/26: 230-4.

_____ 1946. Kälteresistenz und Ernährung. 4. Einfluss des Vitamin C auf die Kälteresistenz. (Cold resistance and nutrition. 4. Effects of vitamin C on cold resistance.) Klin. Wochenschr. 24/25: 40-41.

Graham, G. and E. P. Poulton. 1912. Influence of high temperature on protein metabolism with reference to fever. Quart. J. Med. 6: 82-123.

Granick, S. 1946. Ferritin. IX. Increase of the protein apoferritin in the gastrointestinal mucosa as a direct response to iron feeding. The function of ferritin in the regulation of iron absorption. J. Biol. Chem. 164: 737-46.

Gray, E. LeB., F. C. Consolazio and R. M. Kark. 1947. Nutritional requirements for men at work. QMC-W11-009-qm-70250, Report No. 3, July 31, 25 pp.

Gray, J. S., S. C. F. Mahady and R. L. Masland. 1946. Studies on altitude decompression sickness. III. The effects of denitrogenation. J. Aviation Med. 17: 606-10.

Gray, J. S., H. S. Wigodsky, R. L. Masland and E. L. Green. 1947. Studies on altitude decompression sickness. IV. Attempts to avoid decompression sickness by selection of resistant personnel. J. Aviation Med. 18: 88-95.

Green, D. M. and J. S. Butts. 1945. Factors affecting acceptability of meals served in the air. J. Am. Dietetic Assoc. 21: 415-9.

Green, D. M., J. S. Butts, H. F. Mulholland, with R. M. Moore, R. W. Ollayos, H. B. Griffin, A. B. Shaklee, L. J. Mullins and A. B. Roelofs. 1945. The relationship of anoxia susceptibility to diet. J. Aviation Med. 16: 311-327.

Greene, R. 1941. Frostbite and kindred ills. Lancet ii: 689-93.

Greig, M. E. and W. M. Govier. 1943. Studies on shock induced by hemorrhage. IV. The dephosphorylation of cocarboxylase in tissues during shock and anoxia. J. Pharmacol. Exptl. Therap. 79: 169-75.

Griffie, R. A., G. Chardon and R. Ruffieux. 1942-44. Mechanism of the variation of clotting time in anoxia. Bull. Filiales Soc. Biol. Paris (Soc. biol. Alger) 28-9; Chem. Abs. 39: 4125, 1945.

Griffin, D. R., S. Robinson, H. S. Belding, R. C. Darling and E. S. Turrell. 1946. The effects of cold and rate of ascent on aeroembolism. J. Aviation Med. 17: 56-66.

Grodins, F. S. Effectiveness of a high carbohydrate diet in raising the ceiling of men under the condition of anoxia (SPQRD 430, low protein). VI. The relation of the R.Q. to alveolar oxygen tension. Report to B. E. Proctor, Special Assistant, War Department, Office of the

Quartermaster General (undated) pp. 21-3.

Gross and Romberg. 1943. Untersuchungen am Menschen über den gleichzeitigen Einfluss von Kälte und Sauerstoffmangel. (Investigation of the simultaneous effects of cold and anoxia.) Wright Field Documents. FB 1851, September.

Grosse, A. V. and W. F. Libby. 1947. Cosmic radiocarbon and natural radioactivity of living matter. Science 106: 88-9.

Guerrant, N. B., R. A. Dutcher and R. Crowthers. 1937. Environmental temperature as a factor in the production and in the cure of rickets in the rat. J. Nutrition 14: 471-80.

Gusman, S. M., D. M. Shteingart and K. N. Kharadze. 1945. (Effect of flight on the vitamin metabolism of aviators.) Byull. Eksptl. Biol. Med. 19: 37-40; Chem. Abs. 40: 2213, 1946.

Gustafson, F. L. and F. G. Benedict. 1928. The seasonal variation in basal metabolism. Am. J. Physiol. 86: 43-58.

György, P. 1938. Environmental temperature and 'rat acrodynia.' J. Nutrition 16: 69-77.

Haas, H. T. A. 1939. Ascorbinsäure und Fieber. (Ascorbic acid and fever.) Arch. exptl. Path. Pharm. 192: 331-49.

Hafkesbring, R. and P. Borgstrom. 1926-7. Studies of basal metabolism in New Orleans. Am. J. Physiol. 79: 221-8.

Haggard, H. W. and L. A. Greenberg. 1935. Diet and physical efficiency: The influence of frequency of meals upon physical efficiency and industrial productivity. New Haven: Yale University Press; London: Oxford University Press, 180 pp.

Hailman, H. F. 1944. The effect of vitamins of the B complex on the resistance of the organism to anoxia. Am. J. Physiol. 141: 176-86.

Haldane, J. S. 1927. Acclimatization to high altitudes. Physiol. Rev. 7: 363-84.

Haldi, J., G. Giddings and W. Wynn. 1942. Dietary control of the water content of the skin of the albino rat. Am. J. Physiol. 135: 392-7.

Hall, F. G. 1936. The effect of altitude on the affinity of hemoglobin for oxygen. J. Biol. Chem. 115: 485-90.

Hall, F. G. and J. W. Wilson. 1944. Effects of physical activity and of simulated altitudes on pulmonary ventilation, maximal inspiratory (peak) flow and pressure in relation to oxygen requirements. J. Aviation Med. 15: 160-6.

Hancock, W., A. G. R. Whitehouse and J. S. Haldane. 1929. The loss of water and salts through the skin and the corresponding physiological adjustments. Proc. Roy. Soc. London 105B: 43-59.

Hardt, L. L. and E. U. Still. 1941. Thiamine in sweat. Proc. Soc. Exptl. Biol. Med. 48: 704-7.

Hardy, J. D. and G. F. Soderstrom. 1938. Heat loss from the nude body and peripheral blood flow at temperatures of 22° C. to 35° C. J. Nutrition 16: 493-510.

Harris, A. S. and W. P. Matlock. 1947. The effects of anoxemic anoxia on excitability, conduction and refractoriness of mamalian cardiac muscle. Am. J. Physiol. 150: 493-503.

Harris, M., W. E. Berg, E. M. Whitaker, V. C. Twitty and L. R. Blinks. 1945. CO_2 as a facilitation agent in the initiation and growth of bubbles in animals decompressed to simulated altitudes. J. Gen. Physiol. 28: 225-40.

Harris, S. C., A. C. Ivy and T. E. Friedemann. 1947. Work at high altitude. II. The effect of

training and dietary restriction of thiamine and riboflavin on altitude tolerance and physical efficiency for work at a simulated altitude of 15,000 feet. Quart. Bull. Northwestern University Med. School 21: 135-51.

Hartiala, K. and M. Karvonen. 1946. The influence of anoxia on the gastric HC1-secretion. Acta Physiol. Scand. 11: 85-96.

Hartline, H. K. 1946. Problems of visual physiology during the war. Federation Proc. 5: 351-4.

Hartmann, H. and A. von Muralt. 1934. Blutmilchsäure und Höehenklimawirkung. (Blood lactic acid and the effect of high altitude.) Biochem. Z. 271: 74-88.

Hastings, A. B. and G. Guest. 1944. Summary of report on salt and water requirements to Food and Nutrition Board, National Research Council. National Research Council, Com. Clin. Investigation Rpt. No. 52, June 16.

Haugen, C. O. and G. A. Talbert. 1928. Simultaneous study of the constituents of the sweat, urine and blood: also gastric acidity and other manifestations resulting from sweating. VII. Amino-Acids. Am. J. Physiol. 85: 224-8.

Hausberger, F. X. and N. Nevenschwander-Lemmer. 1939. Beziehungen zwischer Vitamin C-Blutspiegel und Fieberstoffwechsel. (Relation between the vitamin C picture in the blood and fever metabolism.) Klin. Wochschr. 18: 1119-23.

Hecht, S., C. D. Hendley, S. R. Frank and C. Haig. 1946. Anoxia and brightness discrimination. J. Gen. Physiol. 29: 335-51.

Heilbrunn, L. V., D. L. Harris, P. G. Le Fevre, W. L. Wilson and A. A. Woodward. 1946. Heat death, heat injury and toxic factor. Physiol. Zool. 29: 405-29.

Heinbecker, P. 1928. Studies on the metabolism of Eskimos. J. Biol. Chem. 80: 461-75.

Heinbecker, P. 1931. Further studies on the metabolism of Eskimos. J. Biol. Chem. 93: 327-36.

Hemingway, A. and S. R. Hathaway. 1941. An investigation of chemical temperature regulation. Am. J. Physiol. 134: 596-602.

Henderson, C. R., W. B. Bean and W. F. Ashe. 1945. Numerical requirements for statistically valid results in field test of acceptability of rations. Armored Med. Res. Lab., First Supplementary Report on Project No. 30, March 24, 5 pp.

Henry, F. M. and S. F. Cook. 1945. Effectiveness of pre-flight oxygen breathing in preventing decompression sickness. J. Aviation Med. 16: 350-5.

Henschel, A., H. L. Taylor, J. Brozek, O. Mickelsen and A. Keys. 1943. Vitamin C and ability to work in hot environments. OEMcmr-220, Report to Division Med. Res., National Research Council, May 15, 11 pp.

_____ 1944. Vitamin C and ability to work in hot environments. Am. J. Trop. Med. 24: 259-65.

Henschel, A., H. L. Taylor and A. Keys. 1943. The persistence of heat acclimatization in man. Am. J. Physiol. 140: 321-5.

_____ 1944. The gastric emptying time of man at high and normal environmental temperatures. Am. J. Physiol. 141: 205-8.

Henschel, A., H. L. Taylor, O. Mickelsen, J. M. Brozek and A. Keys. 1944. The effect of high vitamin C and B vitamin intakes on the ability of man to work in hot environments. Federation Proc. 3: 18.

Henschel, A., H. L. Taylor, O. Mickelsen and A. Keys. 1943. The effect of high B vitamin intakes on the ability of man to work in the heat. OEMcmr-220, Report to National Research Council, March 11, 4 pp.

Henson, M., D. E. Goldman, H. R. Catchpole, E. P. Vollmer, B. G. King and R. V. Whaley. 1947. Arterial oxygen saturation at altitude. J. Aviation Med. 18: 149-57; 216.

Hermann, H. and F. Jourdan. 1941. Depression barometrique et effects cardiovasculares de l'adrénaline. (Barometric depression and cardiovascular effects of adrenaline.) Compt. Rend. Soc. Biol. 135: 1632-3.

Herrington, L. P. 1940. The heat regulation of small laboratory animals at various environmental temperatures. Am. J. Physiol. 129: 123-39.

Herrlich, H. C., J. F. Fazekas and H. E. Himwich. 1941. Survival of infant and adult rats at high altitudes. Proc. Soc. Exptl. Biol. Med. 48: 446-7.

Herxheimer, H. 1933. Über den Sauerstoffverbrauch bei schwerer Muskelarbeit unter hohen Temperaturen. (Oxygen usage in severe muscular work at high temperatures.) Arbeitsphysiol. 7: 181-92.

Herxheimer, H., R. Kost and K. Ryjaczek. 1933. Untersuchungen über den Gasaustausch im Höhenklima bei leichter und schwerer Muskelarbeit. (The gas exchange in light and severe muscular work at high altitudes.) Arbeitsphysiol. 7: 308-25.

Hier, S. W., T. Cornbleet and O. Bergeim. 1946. The amino acids of human sweat. J. Biol. Chem. 166: 327-33.

Hiestand, W. A. and H. R. Miller. 1944. Further observations on factors influencing hypoxic resistance of mice. Am. J. Physiol. 142: 310-14.

Himwich, H. E., A. O. Bernstein, H. Herrlich, A. Chesler and J. F. Fazekas. 1942. Mechanisms for the maintenance of life in the newborn during anoxia. Am. J. Physiol. 135: 387-91.

Himwich, H. E., J. F. Fazekas, H. C. Herrlich, A. E. Johnson and A. L. Barach. 1942. Studies on the effects of adding carbon dioxide to oxygen-enriched atmospheres in low-pressure chambers. II. The oxygen and carbon dioxide tensions of cerebral blood. J. Aviation Med. 13: 177-81.

Himwich, H. E., J. F. Fazekas and E. Homburger. 1943. Effect of hypoglycemia and anoxia on the survival period of infant and adult rats and cats. Endocrinology 33: 96-101.

Holes, R. and M. G. Larrabee. 1946. The relation between alveolar carbon dioxide tension and susceptibility to decompression sickness. Am. J. Physiol. 147: 603-15.

Hoff, E. C. and C. Yahn. 1944. The effect of sodium 5,5-diphenyl hydantoinate (Dilantin sodium) upon the tolerance of rats and mice to decompression. Am. J. Physiol. 141: 7-16.

Hoffman, C. E., R. T. Clark, Jr. and E. B. Brown, Jr. 1946. Blood oxygen saturations and duration of consciousness in anoxia at high altitudes. Am. J. Physiol. 145: 685-92.

Holt, L. E., Jr. 1943. The B vitamins and certain problems they present to the practical physician. Pennsylvania Med. J. 46: 451-8; Southern Med. and Surgery 105: 9-15.

Hopf, G. 1935. Chemische-physickalische Untersuchungen über den menschlechen Schweiss. (Physiochemical investigations on human sweat.) Arch. Dermatol. Syphilis 171: 301-12.

Hopf, M. 1929. Das Verhalten der Stickstoff- ausscheidung im Urim nach sportlicher Anstrengung im Hochgebirge. (The urinary nitrogen excretion in strenuous sport at high altitudes.) Arbeitsphysiol. 1: 433-65.

Hopps, H. C. and J. H. Lewis. 1947. Studies on capillary permeability as affected by anox-

emia. Am. J. Path. 23: 829-36.

Horstmann, P. 1941. Svedens maelkesyreindhold. (The lactic acid content of sweat.) Nord. Med. 10: 1909-14 (French summary); Nutrition Abs. and Rev. 11: 429, 1942.

Horvath, S. M. and A. Freedman. 1947. The influence of cold upon the efficiency of man. J. Aviation Med. 18: 158-64.

Horvath, S. M., A. Freedman and H. Golden. 1947. Acclimatization to extreme cold. Am. J. Physiol. 150: 99-108.

Horvath, S. M. and W. B. Shelley. 1946. Acclimatization to extreme heat and its effect on the ability to work in less severe environments. Am. J. Physiol. 146: 336-43.

Houghten, F. C., W. W. Teague, W. E. Miller and W. P. Yant. 1931. Heat and moisture losses from men at work and application to air conditioning problems. Heating, Piping and Air Conditioning 3: 493-504.

Houghten, F. C. and C. P. Yagloglou. 1923. Determining lines of equal comfort. Trans. Am. Soc. Heating Ventilating Engns. 29: 163-76.

Houston, C. S. 1946a. The effect of pulmonary ventilation on anoxemia. Am. J. Physiol. 146: 613-21.

_____ 1946b. Operation Everest. A study of acclimatization to anoxia. U. S. Naval Med. Bull. 46: 1783-92.

_____ 1947a. Occurrence of bends, scotomata and hemianopsia at altitudes below 20,000 feet. J. Aviation Med. 18: 165-8.

Houston, C. S. 1947b. The adaptations which produce acclimatization to oxygen lack. J. Aviation Med. 18: 237-43.

Houston, C. S. and R. L. Riley. 1947. Respiratory and circulatory changes during acclimatization to high altitude. Am. J. Physiol. 149: 565-88.

Hove, E. L., K. Hickman and P. L. Harris. 1945. The effect of tocopherol and of fat on the resistance of rats to anoxic anoxia. Arch. Biochem. 8: 395-404.

Hughes, A. M. and E. B. Astwood. 1944. Thyroid function and resistance to anoxia in the rat. J. Aviation Med. 15: 152-7.

Hurtado, A., C. Merino and E. Delgado. 1945. Influence of anoxemia on the hemopoietic activity. Arch. Intern. Med. 75: 284-323.

Hurtado, A., A. Rotta, C. Merino and J. Pons. 1937. Studies of myohemoglobin at high altitudes. Am. J. Med. Sci. 194: 708-13.

Ikemune, I. 1940. The influence of reduced atmospheric pressure on the reflex time. Okayama Igakkai Zassi (Mitt. med. Ges. Okayama) 52: 1270-4 (in German, 1275); Chem. Abs. 37: 1749, 1943.

Isikawa, T. 1939. Changes in blood gases with oxygen deficiency under acid and alkaline conditions. Tohoku J. Expt. Med. 36: 375-410; Chem. Abs. 34: 3344-5, 1940.

Ivy, A. C. 1946. High altitude problems in aviation. Federation Proc. 5: 319-27.

Ivy, A. C., A. J. Atkinson, H. F. Adler and W. L. Burkhardt. 1943. Drugs, diet and bends. OEMcmr-241, Final Bimonthly Report to Com. Med. Res., O.S.R.D., September 1, 5 pp.

Ivy, A. C., A. J. Atkinson, H. F. Adler, W. L. Burkhardt and A. F. Thometz. 1944. Effect of diet, drugs and pressure breathing on bends. OEMcmr-241, Report No. 1, Supplement No. 3

to Com. Med. Res., O.S.R.D., August 1, 3 pp.

Ivy, A. C., C. J. Farmer, L. R. Krasno, S. Freeman, M. W. Burrill, J. H. Boutwell, J. H. Cilley, J. Scow and T. E. Friedemann. 1945. The effect on human subjects of the degree of ascorbic acid deficiency induced and of the disturbance of the metabolism of the vitamin by mild anoxia and its correlation with acid-base disturbances and 17-ketosteroid excretion. Introduction. OEMcmr-236, Final Report of the Com. Aviation Med. to Com. Med. Res., O.S.R.D., June 30, pp. 1-2.

Ivy, A. C., T. E. Friedemann and F. S. Grodins. (undated). Effectiveness of a high carbohydrate diet in raising the ceiling of men under the condition of anoxia (SPQRD 430, low protein). Report to B. E. Proctor, Special Assistant, War Department, Office of the Quartermaster General, pp. 1-4.

Ivy, J. H., F. S. Grodins, H. F. Adler and F. E. Snapp. 1947. Studies on asphyxia. II. Effects of carbon dioxide inhalation on an anoxic animal. J. Aviation Med. 18: 577-89; 622.

Iwamoto, K. 1941. Relation between the vitamin B_1 intake and excretion in high-temperature environment and fever. Kokumin Eisei 18: 23-70; Chem. Abs. 42: 260, 1948.

Jackson, F. K. and A. Alonge. 1934. What constitutes a lethal reduction of temperature? Am. J. Physiol. 109: 447-9.

Jahn, D. and E. Strössenreuther. 1928. Die Abhängigkeit der spezifisch-dynamischen Wirkung von der Ernährungsweise des Menschen. (The dependence of the specific dynamic effect on the kind of diet in man.) Deut. Arch. klin. Med. 159: 152-63.

Jensen, A. V. and H. L. Alt. 1945. Effect of intermittent exposure to simulated high altitude in erythropoiesis in the guinea pig. Proc. Soc. Exptl. Biol. Med. 60: 384-6.

Johnson, B. C., T. S. Hamilton and H. H. Mitchell. 1945a. The effects of choline intake and environmental temperature on the excretion of choline from the human body. J. Biol. Chem. 159: 5-8.

Johnson, B. C., T. S. Hamilton and H. H. Mitchell. 1945b. The excretion of nicotinic acid, nicotinamide, nicotinuric acid, and N^1-methylnicotinamide by normal individuals. J. Biol. Chem. 159: 231-6.

_____ 1945c. The excretion of "folic acid" through the skin and in the urine of normal individuals. J. Biol. Chem. 159: 425-9.

_____ 1945d. The excretion of pyridoxine, "pseudopyridoxine," and 4-pyridoxic acid in the urine and sweat of normal individuals. J. Biol. Chem. 158: 619-23.

Johnson, B. C., H. H. Mitchell and T. S. Hamilton. 1945. The occurrence of inositol and of p-aminobenzoic acid in sweat. J. Biol. Chem. 161: 357-60.

Johnson, R. E. 1943. Nutritional standards for men in tropical climates. Gastroenterology 1: 832-840.

Johnson, R. E., F. C. Consolazio and P. F. Robinson. 1944. Preliminary report on the nutritional aspects of the Canadian Army winter field trials, January and February 1944. Appendix 1. Experiences with pemmican alone and in combination with other foods. Harvard Fatigue Laboratory Report 24 to OQMG, March 10, Appendix 1.

Johnson, R. E. and R. M. Kark. 1947. Environment and food intake in man. Science 105: 378-9.

Johnson, R. E., G. C. Pitts and F. C. Consolazio. 1944. Factors influencing chloride concentration in human sweat. Am. J. Physiol. 141: 575-89.

Johnston, F. A. 1943. The new theory of iron metabolism. J. Am. Dietetic Assoc. 19: 838-40.

Johnston, M. W., J. W. Conn, L. H. Louis and B. F. Steele. 1946. Hand sweat values in the calculation of chloride and nitrogen balance under conditions of hard work in humid heat. Federation Proc. 5: 234.

Jokl, E. 1942. Aviation medicine. London: Sir Isaac Pitman and Sons, Ltd. 213pp.

Jolliffe, N. 1943. The effect of light on production of corneal vascularization and its relation to riboflavin deficiency. OEMcmr-218, Final Report, September 8.

Kaplan, P. M. 1933. Die spezifisch-dynamische Wirkung der gemischten Kost. (The specific dynamic action of mixed foods.) Arbeitsphysiol. 6: 411-32.

Karel, L. and R. E. Weston. 1947. Nitrogen content of femoral arterial and venous blood in anesthetized dogs denitrogenated by continuous inhalation of 99.6 per cent oxygen. Am. J. Physiol. 151: 71-9.

Kark, R. M., H. F. Aiton, E. D. Pease, W. B. Bean, C. R. Henderson, R. E. Johnson and L. M. Richardson. 1947. Tropical deterioration and nutrition. Clinical and biochemical observations on troops. Medicine 26: 1-40.

Kark, R. M., R. E. Johnson and J. S. Lewis. 1945. Defects of pemmican as an emergency ration for infantry troops. War Medicine 7: 345-52.

Kark, R. M., J. F. McCreary, R. E. Johnson, R. R. Melson and L. M. Richardson. 1944. Cold weather operational trials of rations conducted at Prince Albert, Saskatchewan, Canada, January-March, 1944. Ottawa, Canada. Edmond Cloutier.

Karpovich, P. V. and R. R. Ronkin. 1946. Oxygen consumption for men of various sizes in the simulated piloting of a plane. Am. J. Physiol. 146: 394-8.

Kayser, C. 1937. Les lipids assurent préférentiellement la thermogenèse de Rechauffement chez la cobaye. (Lipides are used preferentially for heat production in the chilled guinea pig.) Compt. Rend. Soc. Biol. 126: 701-4.

Keeton, R. W., E. H. Lambert, N. Glickman, H. H. Mitchell, J. H. Last and M. K. Fahnestock. 1946. The tolerance of man to cold as affected by dietary modifications: proteins versus carbohydrates and the effect of variable protective clothing. Am. J. Physiol. 146: 66-83.

Keeton, R. W. and H. H. Mitchell. 1944. The effect of excessive intakes of certain of the water-soluble vitamins on man's resistance to cold. OEMcmr-234, Final Report to Com. Med. Res., O.S.R.D., July, 75 pp.

Kessler, M., H. Hailman and E. Gellhorn. 1943. Studies on the effect of anoxic anoxia on the central nervous system. Am. J. Physiol. 140: 291-8.

Kestner, O. 1921. Klimatologische Studien. I. Der wirksame Anteil des Höhenklimas. (Climatilogical studies. I. The active factor of the climate at high altitudes.) Z. Biol. 73 (N.F. 55): 1-6.

Keys, A. 1943. Diet and fatigue in hot climates. OEMcmr-220, Bimonthly Progress Report No. 6, July 1, 3 pp.

Keys, A., B. H. C. Matthews, W. H. Forbes and R. A. McFarland. 1938. Individual varations in ability to acclimatize to high altitude. Proc. Roy. Soc. London 126B: 1-29.

Keys, A., J. P. Stapp and A. Violante. 1943. Responses in size, output and efficiency of the human heart to acute alteration in the composition of inspired air. Am. J. Physiol. 138: 763-71.

King, C. G. 1943. Studies and experimental investigations in connection with the effects of low oxygen pressure on nutritional requirements. OEMcmr-224, Sum. of Ann. Report to Com. Med. Res., O.S.R.D., October 1, 3 pp.

King, C. G. 1946. Effects of food intake upon resistance to functional impairment during exposure to altitude. OEMcmr-224, Com. Med. Res., O.S.R.D., January, 5 pp.

King, C. G., H. A. Bickerman, W. Bouvet, C. J. Harrer, J. R. Oyler and C. P. Seitz. 1945. Aviation nutrition studies. 1. Effects of pre-flight and in-flight meals of varying composition with respect to carbohydrate, protein and fat. J. Aviation Med. 16: 69-84.

King, C. G., W. Bouvet, M. N. Crood, C. J. Harrer, J. R. Oyler and D. Schwimmer. 1945. Observations on the effect of pre-flight meals upon altitude tolerance. Science 102: 36-8.

Kirch, E. R., T. Cornbleet and O. Bergeim. 1943. Ascorbic acid in sweat. Proc. Soc. Exptl. Biol. Med. 54: 307-8.

Kline, O. L., L. Friedman and E. M. Nelson. 1945. The effect of environmental temperature on thiamine requirement of the rat. J. Nutrition 29: 35-42.

Kline, R. F. 1947a. Effects of severe anoxia and their amelioration. Federation Proc. 6: 143-4.

Kline, R. F. 1947b. Increased tolerance to severe anoxia on carbon dioxide administration. Am. J. Physiol. 151: 538-46.

Knipping, H. W. 1923. Ein Beitrag zur Tropenphysiologie. Untersuchungen des Gaswechsels, der Blutregeneration, des Blutdruckes, der Atemmechanik, des Wärmehaushaltes in des Tropen und der meteorologischen Faktoren des Tropenklimas. Z. Biol. 78: 259-296.

Krasno, L. R., J. H. Cilley, J. H. Boutwell and A. C. Ivy. 1945. The effect on human subjects of the degree of ascorbic acid deficiency induced and of the disturbance of the metabolism of the vitamin by mild anoxia and its correlation with acid-base disturbances and 17-keto-steroid excretion. Part 1. The effect of repeated exposure of human subjects to 18,000 ft. without supplemental oxygen, to hyperventilation, and to 35,000 ft. with 100 pct. oxygen for 1 hour on ascorbic acid excretion and plasma level and on urine pH. OEMcmr-236, Final Report of the Com. Aviation Med. to Com. Med. Res., O.S.R.D., June 30, pp. 3-24.

Krasno, L. R., A. C. Ivy, A. J. Atkinson and W. B. Johnson. 1943. Effect of exposure to anoxia of a moderate degree on the excretion of ascorbic acid in the urine. A preliminary report. War Medicine, Chicago 3: 256-266.

Krauss and Rettig. 1929. Studien zur spezifisch-dynamischen Nahrungswirkung. I. Mitteilung. Die spezifisch-dynamische Eiweisswirkung des normalen erwachsenen Menschen. (Studies on the specific dynamic effect of foods. I. The specific dynamic effect of protein in normal adult men.) Deut. Arch. klin. Med. 163: 337-50.

Kreienberg, W. and D. Gerke. 1942. Der Kohlehydratstoffwechsel bei Sauerstoffmangel. I. Mitteilung. Der Blutzucker. (Carbohydrate metabolism in oxygen deficiency. I. Blood sugar.) Pflüger's Arch. ges. Physiol. 246: 129-39.

Krogh, A. and M. Krogh. 1914-15. A study of the diet and metabolism of Eskimos undertaken in 1908 on an expedition to Greenland. Meddelelser om Gronland 51: 1-52. (in English)

Krotkov, F. G. 1947. Effect of high altitude flying. OQMG, Intelligence Section Planning Branch, Military Planning Division, Dept. of the Army, Washington (translated from Russian October 8, 1947 by W. S. Hurley) p. 1.

Kühnau, W. W. 1939. Experimentelle Untersuchungen über die Beziehungen des Nikotinsäure-amids zum Porphyrinstoffwechsel und zur -Lichtwirkung. (The relation of nicotinamide to porphyrin metabolism and to the action of light.) Strahlentherapie 66: 24-39; Chem. Abs. 34: 812, 1940.

Kuno, Y. 1934. The physiology of human perspiration. London: J. and A. Churchill Ltd., 268 pp.

Kurokawa, G. 1941a. Relation between the high-temperature environment and vitamin A. I. Influence of high-temperature environment upon the appearance of vitamin A avitaminosis. Kokumin Eisei 18: 123-34; Chem. Abs. 42: 260, 1948.

_____ 1941b. Relation between the high-temperature environment and vitamin A. II. Influence of high-temperature environment upon lethal heat-exhaustion. Kokumin Eisei 18: 135-55; Chem. Abs. 42: 260, 1948.

Kuznets, E. I. and V. V. Streltsov. 1947. Does thiouracil affect the resistance to lowered barometric pressure? Byull. Eksptl. Biol. Med. 23: 40-3; Chem. Abs. 41: 6340, 1947.

Ladell, W. S. S. 1945. The effect of desoxycorticosterone acetate on the chloride content of the sweat. J. Physiol. 104: 13-14P.

Ladell, W. S. S., J. C. Waterlow and M. F. Hudson. 1944. Desert climate. Physiological and clinical observations. Lancet 247: 491-7.

Lang, K. 1939. Über die Porphyrinurie im Hochgebirge. (Porphyrinuria in the high mountains.) Biochem. Z. 301: 357-61.

Lang, K. and W. Grab. 1944. Kälteresistenz und Ernährung. (Cold resistance and nutrition.) Klin. Wochenschr. 21/26: 226-30.

Langwill, K. E., C. G. King and G. MacLeod. 1945. Effects of food intake and anoxia upon ascorbic acid excretion, acidity of urine, and survival of male albino rats. J. Nutrition 30: 99-109.

Laugier, H. and C. P. Leblond. 1943. Influence du jeûne et de la réalimentation sur la résistance a l'anoxie. (Effect of fasting and re-feeding on the resistance to anoxia.) Rev. Canadienne Biol. 2: 474-86.

Laurens, H. 1936. Sunlight and health. The Scientific Monthly 42: 312-324.

_____ 1938. The physiological effects of radiation. Physiol. Revs. 8: 1-91.

Laurens, H. and H. S. Mayerson. 1931. The effects of radiant energy on hemorrhagic anemia. J. Nutrition 3: 465-77.

Lawson, F. L. 1942. The effect of sulfanilamide on the ability of rabbits and dogs to withstand high altitudes. Am. J. Physiol. 136: 494-505.

Leblond, C. P. 1944. Increased resistance to anoxia after thyroidectomy and after treatment with thiourea. Proc. Soc. Exptl. Biol. Med. 55: 114-6.

Leblond, C. P., L. P. Dugal and M. Thérien. 1944. Les aliments choisis par le rat blanc au froid et à la chaleur. (The foods chosen by the white rat at low and high temperatures.) Rev. Canadienne Biol. 3: 127-9.

Leblond, C. P., J. Gross and H. Laugier. 1943. Effect of fasting on resistance to anoxia. J. Aviation Med. 14: 262-3; 288.

Leblond, C. P., J. Gross, W. Peacock and R. D. Evans. 1944. Metabolism of radio-iodine in the thyroids of rats exposed to high or low temperatures. Am. J. Physiol. 140: 671-6.

Lee, D. H. K. 1940. A basis for the study of man's reaction to tropical climates. Queensland University Papers 1: No. 5, 86 pp.

Lee, D. H. K., G. H. Klemm and C. White. 1945. Secret report No. 3. Psychomotor efficiency (as measured by time for accurate gun-laying) under hot conditions. National Health and Medical Research Council, Fatigue Laboratory, Sir William Macgregor School of Physiology, University of Queensland, Secret Report No. 3, January 18, 13 pp.

Lee, D. H. K., R. E. Murray, W. J. Simmonds and R. G. Atherton. 1941. The effect of exercise in hot atmospheres upon the salt-water balance of human subjects. Med. J. Australia 28: 249-58.

Lehmann, G. and A. Szakáll. 1937a. Die Bedeutung des Flussigkeitsünd chlorer-satzes für die Leistungsfahigkeit des Hitzearbeiters. (Effect of replenishing fluid and chloride on the capacity for work of workers in hot surroundings.) Arbeitsphysiol. 9: 630-52.

_____ 1937b. Der Chlorstoffwechsel bei Hitzearbeit. (Chloride metabolism during work in hot surroundings:) Arbeitsphysiol. 9: 653-77.

Leipert, T. and E. Kellersmann. 1942. Der Kohlenhydratstoffwechsel in der Hypoxie. I. Hyperglykämische Reaktion. Brenztraubensäure- und Phosphatstoff-wechsel. (Carbohydrate metabolism in hypoxia. I. Hyperglucemic reaction. Pyruvic acid and phosphorus metabolism.) Hoppe-Seyler's Z. Physiol. Chem. 276: 214-32.

Leonhardt, H. 1941. Über den Einfluss thermischer Hautreize auf den Blutzucker-spiegel. (The influence of thermal skin stimuli on the blood sugar.) Deut. Arch. klin. Med. 187: 132.

Levy-Solal, E. and M. Laudat. 1935. Modifications apportées dans la composition du sang de l'individu sain, sous l'influence de la suppression ou de l'addition de sel dans l'alimentation. (Effect of sodium chloride deprivation on the composition of the blood of healthy persons.) Compt. Rend. Soc. Biol. 118: 851-4.

Lewis, R. C., A. Iliff and A. M. Duval. 1943. Further consideration of the effect of altitude on basal metabolism. A study on young women residents of Denver. J. Nutrition 26: 175-85.

Lewis, R. C., A. Iliff, A. M. Duval and G. M. Kinsman. 1943. The effect of change of altitude on the blood of human subjects. J. Lab. Clin. Med. 28: 860-6.

Lewis, R. A., G. W. Thorn, G. F. Koepf and S. S. Dorrance. 1942. The role of the adrenal cortex in acute anoxia. J. Clin. Investigation 21: 33-46.

Li, C. H. and V. V. Herring. 1945. Effect of adrenocorticotropic hormone on the survival of normal rats during anoxia. Am. J. Physiol. 143: 548-51.

Lilienthal, J. L., Jr. 1945. The effect of hyoscine on airsickness. J. Aviation Med. 16: 59-67.

Lilienthal, J. L., Jr., R. L. Riley and D. D. Proemmel. 1946. Arterial oxyhemoglobin saturations at critical pressure-altitudes breathing various mixtures of oxygen and nitrogen: with a note on the effect of exercise. Am. J. Physiol. 145: 427-31.

Lilienthal, J. L., Jr., R. L. Riley, D. D. Proemmel and R. E. Franke. 1946. An experimental analysis in man of the oxygen pressure gradient from alveolar air to arterial blood during rest and exercise at sea level and at altitude. Am. J. Physiol. 147: 199-215.

Lindstedt, H. 1938. Food consumption habits of the Far East. Internat. Rev. Agric. 29: 399E-413E.

List, C. F. 1948. Physiology of sweating. Ann. Rev. Physiol. 10: 387-400.

Lockhart, E. E. 1945. Antarctic trail diet. Proc. Am. Philos. Soc. 89: 235-48.

Loewy, A. 1930. Beobachtungen über den Eiweissabbau in übergrossen Hohen. Ein Beitrag zur Frage nach den Grenzen der akklimatisation an das Höhenklima. (The protein catabolism at extraordinary altitudes. A contribution to the question of the limits of acclimatization of high altitudes.) Arbeitsphysiol. 3: 596-604.

Long, W. H. 1943. The effect of the protein level in the diet on resistance to cold with special reference to the gaseous exchange and the reaction of the body thermostat at low temperatures. Final Report to Com. Med. Res., O.S.R.D., '445 pp.

Lowry, O. H. and O. A. Bessey. 1945. The effects of light, trauma, riboflavin, and aribo-flavinosis on the production of corneal vascularity and on healing of corneal lesions. J. Nutrition 30: 285-92.

Lucas, B. G. B. 1944. Effect of large doses of ascorbic acid on altitude tolerance above 40,000 ft. Com. Flying Personnel Research, Report F PRC-581, April.

Luce-Clausen, E. M. and E. F. Brown. 1939a. The use of isolated radiation in experiments with the rat. II. Effects of darkness, visible and infra-red radiation on three succeeding generations of rat. (a) Growth and storage of vitamin A. J. Nutrition 18: 537-49.

Luce-Clausen, E. M. and E. F. Brown. 1939b. The use of isolated radiation in experiments with the rat. III. Effects of darkness, visible and infra-red radiation on three succeeding generations of rats. (b) Reproduction. J. Nutrition 18: 551-62.

Lundbaek, K. 1944. Fasting values of blood sugar, RQ, and alveolar CO_2 tension on high and low carbohydrate diets. Acta Physiol. Scand. 7: 29-33.

Luyet, B. J. and P. M. Gehenio. 1940. Life and death at low temperatures. Normandy, Missouri: Biodynamica, 341 pp.

MacLachlan, P. L. 1946. Effect of anoxic anoxia on gastric emptying time of rats fed corn oil. Proc. Soc. Exptl. Biol. Med. 63: 147-8.

MacLachlan, P. L. and C. W. Thacker. 1945. The effect of anoxia on fat absorption in rats. Am. J. Physiol. 143: 391-5.

MacPherson, R. K. and D. H. K. Lee. 1945. Secret Report No. 4. The effect of tropical service upon some physical characters of RAAF ground crew (Second report of field investigation into the incidence of tropical fatigue). National Health and Medical Research Council Fatigue Laboratory (Sir William Macgregor School of Physiology, University of Queensland), June 21, 4 pp.

McCance, R. A. 1935-36. Experimental sodium chloride deficiency in man. Proc. Roy. Soc. (London) 119B: 245-68.

_____ 1937. The changes in the plasma and cells during experimental human salt deficiency. Biochem. J. 31: 1278-84.

_____ 1938. The effect of salt deficiency in man on the volume of the extracellular fluids, and on the composition of sweat, saliva, gastric juice and cerebrospinal fluid. J. Physiol. 92: 208-18.

McCance, R. A. and E. M. Widdowson. 1937. The secretion of urine in man during experimental salt deficiency. J. Physiol. 91: 222-31.

McCarrison, R. 1922. Fats in relation to the genesis of goiter. British Med. J. i: 178-81.

_____ 1932. The life line of the thyroid gland. A contribution to the study of goiter. Indian Med. Res. Memoirs No. 23: 378 pp.

McClure, C. W. 1918. The excretion of creatin, creatinin and uric acid in acute febrile conditions. Arch. Intern. Med. 22: 719-49.

McClure, F. J., H. H. Mitchell, T. S. Hamilton and C. A. Kinser. 1945. Balances of fluorine ingested from various sources in food and water by five young men. Excretion of fluorine through the skin. J. Indust. Hygiene and Toxicol. 27: 159-170.

McConnell, W. J., C. P. Yagloglou and W. B. Fulton. 1924. Basal metabolism before and after exposure to high temperatures and various humidities. U. S. Public Health Service, Public Health Repts. 39: 3075-88.

McDonald, R. and F. H. Adler. 1939. Effect of anoxemia on the dark adaptation of the normal and of the vitamin A-deficient subject. Arch. Ophthalmol. 22: 980-87.

McDonough, F. E. 1943. The effect of altitude on gastrointestinal motility. National Research Council, Div. Med. Sci., acting for Com. Med. Res., O.S.R.D., Com. Aviation Med., Abstract of Report No. 213, September 20.

McFarland, R. A. and J. N. Evans. 1939. Alterations in dark adaptation under reduced oxygen tensions. Am. J. Physiol. 127: 37-50.

McFarland, R. A., J. N. Evans and H. M. Halperin. 1941. Opthalmic aspects of acute oxygen deficiency. Arch. Ophthal. 26: 886-913.

McFarland, R. A. and W. H. Forbes. 1940. The effects of variations in the concentration of oxygen and of glucose on dark adaptation. J. Gen. Physiol. 24: 69-98.

McFarland, R. A. and M. H. Halperin. 1940. The relation between foveal visual acuity and illumination under reduced oxygen tension. J. Gen. Physiol. 23: 613-30.

McFarland, R. A., M. H. Halperin and J. I. Niven. 1944. Visual thresholds as an index of physiological imbalance during anoxia. Am. J. Physiol. 142: 328-49.

_____ 1945. Visual thresholds as an index of the modification of the effects of anoxia by glucose. Am. J. Physiol. 144: 378-88.

McFarland, R. A., L. M. Hurvich and M. H. Halperin. 1943. The effect of oxygen deprivation on the relation between stimulus intensity and the latency of visual after-images. Am. J. Physiol. 140: 354-66.

McFarland, R. A., F. J. W. Roughton, M. H. Halperin and J. I. Niven. 1944. The effects of carbon monoxide and altitude on visual thresholds. J. Aviation Med. 15: 381-94.

McIver, M. A., A. C. Redfield and E. B. Benedict. 1926. Gaseous exchange between the blood and the lumen of the stomach and intestine. Am. J. Physiol. 76: 92-111.

McSwiney, B. A. 1934. The composition of human perspiration. Proc. Roy. Soc. Med. 27: 839-48.

Machle, W. 1944. The physiological effects of high temperatures. Military Surgeon 95: 98-105.

Machle, W. and T. F. Hatch. 1947. Heat: man's exchanges and physiological responses. Physiol. Rev. 27: 200-27.

Mackenzie, C. G., A. H. Riesen, J. R. Bailey, T. N. Tahmisian and P. L. Crocker. 1946. Duration of consciousness in anoxia at high altitudes. J. Aviation Med. 16: 156-64; 174.

Mackie, F. P. 1939. Sulfanilamide in the air: A warning. British Med. J. ii: 139.

Maegraith, B. and R. E. Havard. 1946. Anoxia and renal function. Lancet ii: 213-14.

Malméjac, J. 1944. Experimental study on the modifications of urinary secretion at high altitudes. J. Aviation Med. 15: 167-71.

Malméjac, J. and G. Chardon. 1942-44. Effect of barometric depression on intestinal activity. Distinction between chemical and physical factors. Bull. Filial. Soc. Biol. Paris (Soc. biol. Alger), 31; Chem. Abs. 39: 4369-70, 1945.

Malméjac, J., G. Chardon and S. Cruck. 1945. L'élimination urinaire des chlorures au cours de la dépression barométrique. (Urinary elimination of chlorides under reduced barometric pressure.) Compt. Rend. Soc. Biol. 139: 714-15.

Manville, I. A. and E. B. Chase. 1937. The influence of nutritionally produced anemia on the ability of experimental animals to withstand low temperatures. Am. J. Physiol. 118: 549-61.

Marchionini, A. and B. Ottenstein. 1931. Stoffwechselveränderungen im Schwitzbad bei Hautgesunden und Hautkranken. I. Mitteilung. Einfluss auf Säurebasenhaushalt und Mineralstoffwechsel. (Metabolic changes during perspiration in persons with healthy skin and diseased skin. I. Effects upon acid-base economy and mineral metabolism.) Klin. Wochschr. 10: 969-70.

Margaria, R. and L. Faraglia. 1940. Changes in resistance to anoxia provoked by variations in the acid-base balance of the blood. Boll. Soc. Ital. Biol. Sper. 15: 1096-8.

Marshall, L. H. 1946. Respiratory water loss at ground level and altitude. Federation Proc. 5: 71-2.

Martini, E. and C. Torda. 1937. Die Wirkung der hohen Temperatur auf den Ascorbinsäuregehalt der Meerschweinchenorgane. (The effect of high temperatures on the ascorbic acid content of guinea-pig organs.) Klin. Wochschr. 16: 1763-4.

Mason, E. D. 1934. The basal metabolism of European women in South India and the effect of change of climate on European and South Indian women. J. Nutrition 8: 695-713.

_____ 1940. The effect of change of residence from temperate to tropical climate on the basal metabolism, weight, pulse rate, blood pressure, and mouth temperature of 21 English and American women. Am. J. Trop. Med. 20: 669-86.

_____ 1944. Daily measurements of basal metabolism, body temperature and pulse rate during a journey to the tropics. Indian J. Med. Res. 32: 27-30.

Mathews, A. P. 1905. A theory of the nature of protoplasmic respiration and growth. Biological Bull. 8: 331-346.

Matthews, B. H. C. 1932-33. Loss of heat at high altitudes. Proc. Physiol. Soc., J. Physiol. 77: 28P-29P.

Maycock, W. d'A. 1943. Effect of vitamin B_1 on survival time after hemorrhage and application of cold. Quarterly J. Exptl. Physiol. 32: 29-34.

Mayerson, H. S. and H. Laurens. 1928. The effects of carbon arc radiation on the blood of dogs. Am. J. Physiol. 86: 1-14.

Mayerson, H. S. and H. Laurens. 1931. The effects of radiant energy on experimental hemolytic anemia. J. Nutrition 4: 351-62.

Mayr, J. 1943. Haut, Ernährung und Stoffwechsel. Dermatologischer Teil. (Cutaneous nutrition and metabolism.) Arch. Dermatol. Syphilis 184: 155-88.

Meister, W. and W. Hestermann. 1940. Zur Frage des Einflusses der sulfonamide auf die Höhenflugeignung. (The effect of the sulfonamides on adaptation to altitude flying.) Klin. Wochschr. 19: 1080-2.

Mellanby, E. and M. Mellanby. 1921. The experimental production of thyroid hyperplasia in dogs. J. Physiol. 55: vii-viii.

Merény, G. S. v., Z. Korényi and H. Gordon. 1944. Über die Steigerung der Höhenfestigkeit durch wiederholte U-Kammeraufstiege. (The increase in resistance to altitude after repeated sojourns in the low pressure chamber.) Luftfahrtmed. 8: 331-8.

Michel, H. O. and I. H. Scheinberg. 1947. The effects of cytochrome c on anoxic and cyanide-poisoned rats. J. Biol. Chem. 169: 277-86.

Mickelsen, O. and A. Keys. 1943. The composition of sweat, with special reference to the

vitamins. J. Biol. Chem. 149: 479-90.

Miller, W. N., P. Anderson and A. Dorfman. 1948. Effect of anoxia and cytochrome C on readily hydrolyzable phosphate of rat tissues. Science 107: 421.

Mills, C. A. 1941. Environmental temperatures and thiamine requirements. Am. J. Physiol. 133: 525-31.

_____ 1942. Environmental temperature and B-vitamin requirements. Arch. Biochem. 1: 73-81.

_____ 1943a. Environmental temperatures and B-vitamin requirements: riboflavin and pyridoxine. Arch Biochem. 2: 159-62.

_____ 1943b. Heightened thiamine and choline requirements in tropical heat. Proc. Soc. Exptl. Biol. Med. 54: 265-6.

_____ 1944. Metabolic acclimatization to tropical heat. Proc. Central Soc. Clin. Res. 17: 12-13.

Mills, C. A., E. Cottingham and M. Mills. 1944. Environmental temperature and vitamin K deficiency. Am. J. Physiol. 141: 359-62.

Mills, C. A., E. Cottingham and E. Taylor. 1947. The influence of environmental temperature on dietary requirement for thiamine, pyridoxine, nicotinic acid, folic acid and choline in chicks. Am. J. Physiol. 149: 376-82.

Mitchell, H. H., N. Glickman, E. H. Lambert, R. W. Keeton and M. K. Fahnestock. 1946. The tolerance of man to cold as affected by dietary modification: carbohydrate versus fat and the effect of the frequency of meals. Am. J. Physiol. 146: 84-96.

Mitchell, H. H., T. S. Hamilton, J. B. Shields and W. T. Haines. 1943. The effect of high environmental temperatures, varied humidities, and moderate muscular work on the losses of water-soluble vitamins and of minerals in the perspiration of adult human subjects. OEMcmr-227, Interim Report, O.S.R.D., August, 38 pp.

Molchanova, O. P. 1941. Effect of repeated exposure to low barometric pressure on metabolism and the acid-alkaline balance. Voprosy Pitaniya 10: 7-14; Chem. Abs. 40: 387, 1946.

Molnar, G. W. 1946. Survival of hypothermia by men immersed in the ocean. J. Am. Med. Assoc. 131: 1046-50.

Molnar, G. W., E. J. Towbin, R. E. Gosselin, A. H. Brown and E. F. Adolph. 1946. Water, salt, and heat exchange of men in tropical and desert environments. Am. J. Hygiene 44: 411-33.

Molomut, N. and S. C. Allen. 1946. Effect of pressure breathing on circulation at high altitude as measured by the ballistocardiograph. J. Aviation Med. 17: 357-63.

Morton, T. C. 1944. Heat effects in British service personnel in Iraq. Trans. Roy. Soc. Trop. Med. Hygiene 37: 347-62.

Mosher, H. H. 1933. Simultaneous study of constituents of urine and perspiration. J. Biol. Chem. 99: 781-90.

Motley, H. L., H. I. Chinn and F. A. Odell. 1945. Studies on bends. J. Aviation Med. 16: 210-34.

Muido, L. 1946. The influence of anoxia on the eye hand coordination. Acta Physiol. Scand. 12: 99-101 (in English).

Murlin, J. R., A. C. Burton and W. M. Barrows, Jr. 1936. The specific dynamic action of butterfat and of super-imposed sugar. J. Nutrition 12: 613-44.

Murray, H. C. and A. F. Morgan. 1946. Carbohydrate metabolism in the ascorbic acid-deficient guinea pig under normal and anoxic conditions. J. Biol. Chem. 163: 401-10.

Myers, V. C. and G. O. Volovic. 1913. The influence of fever on the elimination of creatinine. J. Biol. Chem. 14: 489-508.

Mylon, E. and A. E. Wilhelmi. 1945. Relation of food intake to the resistance of liver to anoxia. OEMcmr-341, Progress Report No. 11, April 15; Abstr. in Sum. of Reports, Com. Med. Res., O.S.R.D., April 16-21, 1945; Bull. 38: 461.

Nastuk, W. L. 1947. Changes in certain phosphorus and carbohydrate constituents of the tissues of rabbits in gravity shock. Am. J. Physiol. 149: 369-375.

Naval Medical Research Institute. 1945. Self selection of diets in rats rendered anoxic by decompression to altitude. I. Salt appetite. Naval Medical Research Institute, Nat'l. Naval Med. Center, Research Proj. X-316, Rpt. No. 1, November 27.

Nelson, D., S. Goetzl, S. Robins and A. C. Ivy. 1943. Carrot diet and susceptibility to acute "anoxia." Proc. Soc. Exptl. Biol. Med. 52: 1-2.

Nelson, N. and W. B. Bean. 1942. Water and salt requirements for desert operations. Armored Medical Research Laboratory, Fort Knox, Kentucky, Project No. 2-6, Partial Report, November 12.

Newburgh, L. H. and M. Harris (Editors). 1945. Clothing test methods. National Research Council, Committee on Aviation Medicine, Report No. 390: 98 pp.

Nicholls, L. 1938. Tropical nutrition and dietetics. London: Bailiere, Tindall and Cox, 164 pp.

Nims, L. F., L. L. Langley and R. W. Clarke. 1946. Anoxia, carbon dioxide and liver glycogen. Federation Proc. 5: 76-7.

Nims, L. F. and F. Olmstead. 1945. Oxygen consumption under basal conditions at sea level and at 30,000 ft. OEMcmr-38, Interim Report, Special Com. Aviation Med. Report, September 4, N.R.C. No. 13, 284 pp.

Northup, D. W. and E. J. Van Liere. 1939. Intestinal secretion during anoxia. Proc. Soc. Exptl. Biol. Med. 42: 162-3.

_____ 1941. The effect of anoxia on the absorption of glucose and of glycine from the small intestine. Am. J. Physiol. 134: 288-91.

Nyman, E. and A. Palmlöv. 1936. The elimination of ethyl alcohol in sweat. Skand. Arch. Physiol. 74: 155-9.

O'Connor, J. M. 1942. The influence of fatty acids on the oxygen consumption of the tissues in relation to temperature and the theory of temperature regulation. Proc. Roy. Irish Acad. 48B: 93-103.

O'Connor, J. M. and D. K. O'Donovan. 1942. The influence of temperature on animal oxidation Proc. Roy. Irish Acad. 47B: 251-64.

Olevskii, M. I., L. L. Zelenko and S. T. Kuz'menko. 1936. Effect of low external temperature on the activity of the gastrointestinal tract. Méd. Exptl. (Ukraine) No. 8, 37-47; Chem. Abs. 31: 1475, 1937.

Opitz, E. and F. Palme. 1944. Darstellung der Höhenanpassung im Gebirge durch Sauerstoffmangel. II. Mitteilung. Atmung und kritische alveolare Sauerstoffspannung bei Rückatmung

im Gebirge. (Adaptation to high altitude in the mountains through oxygen deficiency. II. Respiration and critical alveolar oxygen tension in rebreathing [studies] in the mountains.) Pflüger's Arch. ges. Physiol. 248: 298-329.

Oppel, T. W. and J. D. Hardy. 1937. Studies in temperature sensation. I. A comparison of the sensation produced by infra-red and visible radiation. J. Clin. Investigation 16: 517-24.

Osborne, S. L. and C. J. Farmer. 1942. Influence of hyperpyrexia on ascorbic acid concentration in the blood. Proc. Soc. Exptl. Biol. Med. 49: 575-8.

Oster, R. H. and D. C. Smith. 1947. The influence of adrenalin on blood sugar and resistance to hypoxia in the nembutalized cat. Am. J. Physiol. 150: 321-4.

Otis, A. B., H. Rahn, M. A. Epstein and W. O. Fenn. 1946. Performance as related to composition of alveolar air. Am. J. Physiol. 146: 207-21.

Pace, N., E. L. Lozner, W. V. Consolazio, G. C. Pitts and L. J. Pecora. 1947. The increase in hypoxia tolerance of normal men accompanying the polycythemia induced by transfusion of erythrocytes. J. Am. Physiol. 148: 152-63.

Packard, W. H. 1907. The effect of carbohydrates on resistance to lack of oxygen. Am. J. Physiol. 18: 164-180.

Peterson, E. W., M. B. Bornstein and H. H. Jasper. 1945a. Effect of morphine sulfate on persons exposed to simulated altitude. War. Med. 7: 23-8.

Peterson, E. W., M. B. Bornstein and H. H. Jasper. 1945b. Effect of sulfathiazole on persons subjected to simulated altitude. War Med. 7: 29-31.

Peterson, J. M. 1941. Ascorbic acid and resistance to low oxygen tension. Nature 148: 84.

Pickett, A. D. and E. J. Van Liere. 1939. The effect of anoxia on gastric secretion from Pavlov and Heidenhain pouch dogs. Am. J. Physiol. 127: 637-41.

Pincus, G. and H. Hoagland. 1943. Steroid excretion and the stress of flying. J. Aviation Med. 14: 173-93.

Pitts, G. C., F. C. Consolazio and R. E. Johnson. 1944. Dietary protein and physical fitness in temperate and hot environments. J. Nutrition 27: 497-508.

Pitts, G. C., R. E. Johnson and F. C. Consolazio. 1944. Work in the heat as affected by intake of water, salt and glucose. Am. J. Physiol. 142: 253-9.

Pogrund, R. S. 1947. Studies on gaseous transfer between the colon and blood stream in man. Thesis, University of Illinois. 73 pp.

Polonovski, M. 1940. Effect of sugar ingestion on resistance to anoxemia and acapnia at high altitudes. Bull. Acad. Med. 123: 688-94.

_____ 1943. Influence de l'hypoxémia sur l'élimination urinaire des phosphates. (Influence of hypoxemia on urinary elimination of phosphates.) Compt. Rend. Soc. Biol. 137: 37-8.

Potter, V. R. 1947. (Current interest in the therapeutic use of cytochrome c.) Science 106: 342.

Proger, S. and D. Dekaneas. 1946. The use of cytochrome c in combating tissue anoxia. Science 104: 389-90.

Proger, S., D. De(k)aneas and G. Schmidt. 1945a. The effects of anoxia and of injected cytochrome-c on the content of easily hydrolyzable phosphorus in rat organs. J. Biol. Chem. 160: 233-238.

Proger, S., D. Dekaneas and G. Schmidt. 1945b. Some observations on the effect of injected cytochrome C in animals. J. Clin. Investigation 24: 864-8.

Quastel, J. H. and E. Racker. 1941. Tissue anoxia and blood coagulation. Brit. J. Exptl. Path. 22: 15-17.

Radsma, W. and Nizar. 1938. On the excretion of lactic acid by the skin. Acta Brevia Neerland. Physiol. Pharmacol. Microbiol. (in English) 8: 147-9.

Rafsky, H. A. and B. Newman. 1943. Relationship of niacin (nicotinic acid) to porphyrinuria in the aged. Am. J. Med. Sci. 205: 209-213.

Rahn, H. and A. B. Otis. 1947. Alveolar air during simulated flights to high altitudes. Am. J. Physiol. 150: 202-21.

Rahn, H., A. B. Otis, L. E. Chadwick and W. O. Fenn. 1946. The pressure-volume diagram of the thorax and lung. Am. J. Physiol. 146: 161-178.

Reed, A. C. 1942. Tropical neurasthenia. Am. J. Trop. Med. 22: 127-30.

Remington, R. E. 1938. Does fat in the diet affect the thyroid? J. Nutrition 16: 417-24.

Reynolds, O. E. 1947. The effect of discontinuous chronic anoxia on liver glycogen stores. Am. J. Physiol. 150: 65-6.

Reynolds, O. E. and N. E. Phillips. 1947. Adaptation of the albino rat to discontinuous chronic exposure to altitude anoxia. Am. J. Physiol. 151: 147-54.

Riesen, A. H., T. N. Tahmisian and C. G. Mackenzie. 1946. Prolongation of consciousness in anoxia of high altitude by glucose. Proc. Soc. Exptl. Biol. Med. 63: 250-4.

Ring, G. C. 1942. The importance of the thyroid in maintaining an adequate production of heat during exposure to cold. Am. J. Physiol. 137: 582-8.

Robinson, K. W. and D. H. K. Lee. 1947. The effect of the nutritional plane upon the reactions of animals to heat. J. Animal Sci. 6: 182-194.

Robinson, S. 1942. The effect of body size upon energy exchange in work. Am. J. Physiol. 136: 363-8.

Robinson, S. and S. D. Gerking. 1947. Thermal balance of men working in severe heat. Am. J. Physiol. 149: 476-88.

Robinson, S., E. S. Turrell, H. S. Belding and S. M. Horvath. 1943. Rapid acclimatization to work in hot climates. Am. J. Physiol. 140: 168-76.

Robinson, W. B. 1943. The effect of environmental temperature on the thiamine requirement of the growing albino rat. Ph. D. Thesis. University of Illinois, 68 pp.

Rodbard, S. 1947a. Relationship between body temperature and blood sugar in the chicken. Am. J. Physiol. 150: 67-9.

_____ 1947b. Studies on the recurrence of decompression sickness on re-ascent to high altitudes. Am. J. Physiol. 150: 133-41.

Rose, H. and I. Schmidt. 1947. Beeinflussung der Dunkeladaptation. (Factors affecting dark adaptation.) J. Aviation Med. 18: 218-30; 243. (in English)

Rosenthal, O., H. Shenkin and D. L. Drabkin. 1945. Oxidation of pyruvate and glucose in brain suspensions from animals subjected to irreversible hemorrhagic shock, carbon monoxide poisoning, or temporary arrest of the circulation--a study of the effects of anoxia. Am. J. Physiol. 144: 334-47.

Rowland, W. M. and L. L. Sloan. 1945. Night blindness in flying personnel. Observations on patients studied at the AAF School of Aviation Medicine. J. Aviation Med. 16: 49-58.

Rubner, M. 1902. Die Gesetze des Energieverbrauchs bei der Ernährung. (The precept of transformation of energy in nutrition.) Leipzig and Vienna.

Ruff, S. and H. Strughold. 1942. Compendium of aviation medicine. Washington, D. C.: National Research Council; English translation, 130 pp.

Rühl, A. 1943. Über die Möglichkeiten einer Steigerung der menschlichen Höhenfestigkeit durch therapeutische Massnahmen. (Possible improvement of human altitude tolerance by therapeutic means.) Deut. med. Wochschr. 69: 25-8.

Rushmer, R. F., E. L. Beckman and D. Lee. 1947. Protection of the cerebral circulation by the cerebrospinal fluid under the influence of radial acceleration. Am. J. Physiol. 151: 355-65.

Sacerdote, P. 1938a. Variations du taux de l'acide ascorbique du sang et des tissus au cours de l'anoxémie. (Variations in the ascorbic acid content of the blood and tissues during anoxaemia.) Ann. Physiol. Physicochim. biol. 14: 271-286; Nutrition Abs. Rev. 8: 391-92, 1938.

_____ 1938b. L'acido ascorbico nell'anossiemia. (Ascorbic acid in anoxaemia.) Boll. Soc. ital. Biol. sper. 13: 847-850; Nutrition Abs. Rev. 8: 649, 1939.

Samaras, K. 1939. Der Einfluss der Kälte auf den Kohlehydratstoffwechsel. (The effect of cold on carbohydrate metabolism.) Z. ges. exptl. Med. 106: 510-20.

Sankaran, G. and K. Rajagopal. 1938. Haematological investigations in South India. V. The effect of altitude on haemoglobin content. Indian J. Med. Res. 25: 971-77.

Sarett, H. P. and W. A. Perlzweig. 1943. The effect of high temperature and B-vitamin levels of the diet upon the metabolism and body composition of rats. J. Nutrition 26: 611-20.

Sargent, F., P. Robinson and R. E. Johnson. 1944. Water-soluble vitamins in sweat. J. Biol. Chem. 153: 285-94.

Scheinberg, I. H. and H. O. Michel. 1947. The effects of cytochrome C in anoxia. Science 105: 365-6.

Scheiniss, B. (Moscow, Military Acad. Med.). 1943. Death from exposure to cold. Moscow. (Taken from Lancet ii: 319, 1944.)

Schmidt, H. 1939. Work experiments in oxygen deficiency. Industr. Psychotechn. 16: 137; Zentr. Gewerbehyg. Unfallverhüt. 27: 170, 1940.

Schmidt-Nielsen, K. 1946. Melting points of human fats as related to their location in the body. Acta Physiol. Scand. 12: 123-9. (in English)

Schneider, E. C. 1921. Physiological effects of altitude. Physiol. Rev. 1: 631-59.

Schneider, E. C. and R. W. Clarke. 1929. Studies of muscular exercise under low barometric pressure. IV. The pulse rate, arterial blood pressure and oxygen pulse. Am. J. Physiol. 88: 633-49.

Schneider, W. 1946. Ätiologie und Pathogenese der Kälteschäden der Haut. (Aetiology and pathogenesis of cutaneous affections due to cold.) Arch. Dermotol. Syphlol. 186: 3-31.

Schoenheimer, R. and D. Rittenberg. 1935. Deuterium as an indicator in the study of intermediary metabolism. III. The role of the fat tissues. J. Biol. Chem. 111: 175-181.

Selle, W. A. 1944. Influence of glucose on the gasping pattern of young animals subjected to acute anoxia. Am. J. Physiol. 141: 297-302.

Shaffer, P. 1908. The excretion of kreatinin and kreatin in health and disease. Am. J. Physiol. 23: 1-22.

Sherman, H. C. 1945. Chemistry of food and nutrition. New York, 7th ed., 675 pp.

Shields, J. B., B. C. Johnson, T. S. Hamilton and H. H. Mitchell. 1945. The excretion of ascorbic acid and dehydroascorbic acid in sweat and urine under different environmental conditions. J. Biol. Chem. 161: 351-6.

Silvette, H. 1943. Some effects of low barometric pressures on kidney function in the white rat. Am. J. Physiol. 140: 374-86.

Sinclair, R. D. 1933. Influence of radiant energy on the hematopoietic processes in the pig. Sci. Agric. 13: 737-42.

Siple, P. A. 1945. General principles governing selection of clothing for cold climates. Proc. Am. Philos. Soc. 89: 200-34.

Skarland, I. 1947. Personal Communication, November 4.

Slater, E. C. 1942. Thiamine content of sweat. Australian J. Sci. 4: 136.

Sleeth, C. K. and E. J. Van Liere. 1937a. The effect of environmental temperature on the emptying time of the stomach. Am. J. Physiol. 118: 272-5.

_____ 1937b. Effect of anoxemia on the impermeability of the stomach to water. Proc. Soc. Exptl. Biol. Med. 36: 571-3.

Smedal, H. A., E. B. Brown, Jr. and C. E. Hoffman. 1946. Incidence of bends pain in a short exposure to simulated altitudes of 26,000, 28,000 and 30,000 feet. J. Aviation Med. 17: 67-9; 79.

Smith, D. T. and J. M. Ruffin. 1937. Effect of sunlight on the clinical manifestations of pellagra. Arch. Intern. Med. 59: 631-45.

Smith, D. C. and R. H. Oster. 1946. Influence of blood sugar levels on resistance to low oxygen tension in the cat. Am. J. Physiol. 146: 26-32.

Smith, D. C., R. H. Oster and J. E. P. Toman. 1944. The effect of thiamine deficiency and of reduced food intake on resistance to low oxygen tension in the cat. Am. J. Physiol. 140: 603-8.

Smith, G. M., C. P. Seitz and K. B. Clark. 1946. Variations in the angioscotoma in response to prolonged mild anoxia. J. Aviation Med. 17: 590-5.

Smith, H. P., A. E. Belt, H. R. Arnold and E. B. Carrier. 1924-5. Blood volume changes at high altitude. Am. J. Physiol. 71: 395-412.

Smith, P. K. 1946a. Studies of the effects of morphine at simulated high altitudes and its use for the relief of pain of decompression sickness. J. Aviation Med. 17: 265-9.

_____ 1946b. The effectiveness of some motion sickness remedies in preventing air sickness in air force navigation students. J. Aviation Med. 17: 343-5.

_____ 1946c. Use of hyoscine hydrobromide for the prevention of airsickness in flexible gunnery students. J. Aviation Med. 17: 346-7.

_____ 1946d. Effect of various substances on swing sickness. Proc. Soc. Exptl. Biol. Med. 63: 209-10.

Smith, P. K. and A. Hemingway. 1946. Effect of some atropine-like drugs on swing sickness. Proc. Soc. Exptl. Biol. Med. 63: 206-8.

Snapper, I. and A. Grünbaum. 1929. Über Milchsäurcausscheidung im Harn und Schweiss bei verschiedenen Sportarten. (On lactic acid excretion in urine and sweat with different kinds of sports.) Biochem. Z. 208: 212-20.

Soderstrom, G. F., D. P. Barr and E. F. DuBois. 1918. Clinical calorimetry. XXVI. The effect of a small breakfast on heat production. Arch. Intern. Med. 21: 613-620.

Spealman, C. R. 1945a. A characteristic of human temperature regulation. Proc. Soc. Exptl. Biol. Med. 60: 11-12.

_____ 1945b. The effectiveness of partial immersion and periodic immersion in water for cooling men in hot spaces. Naval Med. Research Institute, Research Project x-552, August 15, 4 pp.

_____ 1946. Body cooling of rats, rabbits and dogs following immersion in water, with a few observations on man. Am. J. Physiol. 146: 262-6.

Spector, H., T. S. Hamilton and H. H. Mitchell. 1945. The effect of pantothenic acid dosage and environmental temperature and humidity upon the dermal and renal excretion of pantothenic acid. J. Biol. Chem. 161: 145-52.

Spector, H., H. H. Mitchell and T. S. Hamilton. 1945. The effect of environmental temperature and potassium iodide supplementation on the excretion of iodine by normal human subjects. J. Biol. Chem. 161: 137-43.

Starr, P. and R. Roskelley. 1940. A comparison of the effects of cold and thyrotropic hormone on the thyroid gland. Am. J. Physiol. 130: 549-56.

Stefansson, V. 1944a. Arctic manual. New York: MacMillan Co., 556 pp.

Stefansson, V. 1944b. The diets of explorers. Military Surgeon 95: 1-3.

_____ 1944c. Pemmican. Military Surgeon 95: 89-98.

Stevens, C. D., H. W. Ryder and E. B. Ferris. 1947. The rate of nitrogen elimination through the lungs in relation to susceptibility to decompression sickness. Federation Proc. 6: 400.

Stevens, C. D., H. W. Ryder, E. B. Ferris and M. Inatome. 1947. The rate of nitrogen elimination from the body through the lungs. J. Aviation Med. 18: 111-32; 168.

Stickney, J. C. and E. J. Van Liere. 1942a. Acclimatization to low oxygen tensions in relation to gastric emptying. Am. J. Physiol. 137: 160-3.

_____ 1942b. Erythrocytes and hemoglobin values in acclimatization produced by discontinuous anoxia. J. Aviation Med. 13: 170-6.

Stillman, H. A. and M. Lawrence. 1925. The effects of external temperature on the basal metabolism of young women under usual conditions of dress. Missouri Experiment Station Bull. 228: 65 pp.

Streltsov, V. 1944. The function of the eye in aviation. Am. Rev. Soviet Med. 2: 126-33.

Sundstroem, E. S. 1919. Studies on the adaptation of man to high altitudes. II. Effect of high altitudes on protein metabolism. University of California Publ. Physiol. 5: 87-104.

_____ 1926. Contributions to tropical physiology with special reference to the adaptation of the white man to the climate of North Queensland. University of California Publ. Physiol. 6: 1-216.

Swift, R. W. 1932. The effects of low environmental temperature upon metabolism. I. Technic and respiratory quotient. J. Nutrition 5: 213-225.

_____ 1944. The effect of feed on the critical temperature for the albino rat. J. Nutrition 28: 359-364.

Talbert, G. A., J. R. Finkle and S. S. Katsuki. 1927. Simultaneous study of the constituents of the sweat, urine and blood, also gastric acidity and other manifestations resulting from sweating. III. Urea. Am. J. Physiol. 82: 153-6.

Talbert, G. A., C. Haugen, R. Carpenter and J. E. Bryant. 1933. Simultaneous study of the constituents of the sweat, urine and blood; also gastric acidity and other manifestations resulting from sweating. X. Basic metals. Am. J. Physiol. 104: 441-2.

Talbert, G. A., S. Silvers and W. Johnson. 1927. Simultaneous study of the constituents of the sweat, urine and blood, also gastric acidity and other manifestations resulting from sweating. II. Total nitrogen of sweat and urine; total non-protein nitrogen of blood. Am. J. Physiol. 81: 81-85.

Talbert, G. A., F. Stinchfield and H. Staff. 1933. Simultaneous study of the constituents of the sweat, urine and blood; also gastric acidity and other manifestations resulting from sweating. XI. Phosphorus and sulphur. Am. J. Physiol. 106: 488-90.

Talbott, J. H. 1944a. Cold exposure: Pathologic effects. Medical Physics, Otto Glasser, editor, 244-6 pp.

_____ 1944b. Heat: pathologic effects. Medical Physics, Year Book Publishers, Inc., Chicago, edited by Otto Glasser, pp. 588-91.

Taylor, C. L. 1946. Physical exertion in the heat: some notes on its physiology and hygiene. J. Aviation Med. 17: 137-45; 191.

Taylor, H. L., A. F. Henschel and A. Keys. 1943. Cardiovascular adjustments of man in rest and work during exposure to dry heat. Am. J. Physiol. 139: 583-91.

Taylor, H. L., A. Henschel, O. Mickelsen and A. Keys. 1943. The effect of the sodium chloride intake on the work performance of man during exposure to dry heat and experimental heat exhaustion. Am. J. Physiol. 140: 439-51.

Tennent, D. M. and R. H. Silber. 1943. The excretion of ascorbic acid, thiamine, riboflavin and pantothenic acid in sweat. J. Biol. Chem. 148: 359-64.

Thomas, W. A. 1927. Health of a carnivorous race. A study of the Eskimo. J. Am. Med. Assoc. 88: 1559-60.

Thompson, J. W., C. B. Stewart, O. H. Warwick, G. L. Bateman, D. J. Milne and D. E. Gray. 1944. Relation of certain factors to the incidence of decompression sickness. Proc. 16th Meeting of the Associate Com. Medical Research, National Research Council, Canada, C-2064, April 25.

Thorn, G. W., M. Clinton, Jr., B. M. Davis and R. A. Lewis. 1945. Effect of adrenal cortical hormone therapy on altitude tolerance. Endocrinology 36: 381-90.

Thorn, G. W., B. F. Jones, R. A. Lewis, E. R. Mitchell and G. F. Koepf. 1942. The role of the adrenal cortex in anoxia: The effect of repeated daily exposures to reduced oxygen pressure. Am. J. Physiol. 137: 606-19.

Tourtellotte, D. and W. E. Bacon. 1935. Variability of vitamin D response with temperature of environment. J. Nutrition 10: 683-8.

Treichler, R. and H. H. Mitchell. 1941. The influence of plane of nutrition and of environmental temperature on the relationship between basal metabolism and endogenous nitrogen

metabolism subsequently determined. J. Nutrition 22: 333-43.

Tsamboulas, N. 1939. Die spezifisch-dynamische Wirkung der Nährstoffe bei verschieden ernährten Personen. (The specific dynamic action of nutrients in differently nourished individuals.) Z. klin. Med. 136: 327-33.

Tyslowitz, R. and E. B. Astwood. 1942. The influence of the pituitary and adrenal cortex on resistance to low environmental temperatures. Am. J. Physiol. 136: 22-31.

Van Liere, E. J. 1937. Effect of anoxemia on the emptying time of the human stomach. Influence of high altitudes. Arch. Intern. Med. 58: 130-5.

_____1941. The effect of anoxia on the alimentary tract. Physiol. Rev. 21: 307-23.

_____1942. Anoxia: Its effects on the body. Chicago: The University of Chicago Press, 254 pp.

Van Liere, E. J., N. A. David and D. H. Lough. 1936. Absorption of water from the small intestine at various degrees of anoxemia. Am. J. Physiol. 115: 239-44.

Van Liere, E. J., D. W. Northup and J. C. Stickney, 1944. The effect of anoxic and anemic anoxia on the motility of the small intestine and the influence of an epinephrine-potentiating-agent. Am. J. Physiol. 142: 615-20.

Van Liere, E. J., D. W. Northup, J. C. Stickney and G. A. Emerson. 1943. The effect of anoxia on peristalsis of the small and large intestine. Am. J. Physiol. 140: 119-23.

Van Liere, E. J., D. W. Northup, J. C. Stickney and R. E. Richard. 1947. Effect of anemic anoxia on absorption of isotonic magnesium sulfate from the small intestine. Proc. Soc. Exptl. Biol. and Med. 64: 62-4.

Van Liere, E. J., H. S. Parker, G. R. Crisler and J. E. Hall. 1935-36. Effect of anoxemia on secretion of urine in the dog. Proc. Soc. Exptl. Biol. Med. 33: 479-80.

Van Liere E. J. and C. K. Sleeth. 1936. Absorption of sodium chloride from the small intestine at various degrees of anoxemia. Am. J. Physiol. 117: 309-12.

Van Liere, E. J. and P. E. Vaughan. 1940. The influence of anoxia on the absorption of sodium chloride and sodium sulphate from the small intestine. Am. J. Physiol. 129: 618-22.

_____1941. Basal secretion of Pavlov pouch dogs as influenced by oxygen want. Am. J. Digestive Diseases 8: 155-6.

Van Middlesworth, L. 1944. Carbohydrate ingestion during severe anoxia. Proc. Virginia Acad. Sci., pp. 50-1.

_____1946. Glucose ingestion during severe anoxia. Am. J. Physiol. 146: 491-5.

Van Middlesworth, L., R. F. Kline and S. W. Britton. 1944. Carbohydrate regulation under severe anoxic conditions. Am. J. Physiol. 140: 474-82.

Vannotti, A. and H. Markwalder. 1939. Blutumsatz und Hochgebirge. (Erythropoiesis at high altitudes.) Z. ges. exptl. Med. 105: 1-13; Chem. Abs. 34: 3794, 1940.

Van Veen, A. G. 1942. Nutrition. Ann. Rev. Biochem. 11: 391-409.

Vernon, H. M. 1923. The index of comfort at high atmospheric temperatures. Privy Council, Medical Research Council (London), Spec. Rpt. Series No. 73, Part V, pp. 116-44.

Vladimirov, G. E., N. F. Grigor'ev, I. M. Dedyulin, L. I. Ostrogorskaya and I. I. Fedorov. 1945. A food regime for high altitudes. J. Physiol. U. S. S. R. 31: 356-63.

Voit, K. 1933. Untersuchungen über den Kohlenstoff- und Stickstoffgehalt des menschlichen Schweisses. (Studies on the carbon and nitrogen contents of human sweat.) Deut. Arch. Klin. Med. 175: 108-114.

Wachholder, K. and H. Franz. 1944. Die spezifisch-dynamische Stoffwechselsteigerung bei gemischter Kost. (The specific dynamic action of a mixed diet.) Pflüger's Arch. ges. Physiol. 247: 632-48.

Wald, G., P. V. Harper, Jr., H. C. Goodman and H. P. Kreiger. 1942. Respiratory effects upon visual threshold. J. Gen. Physiol. 25: 891-903.

Waterman, R. E. and M. Ammerman. 1935a. Studies of crystalline vitamin B. V. The effect of graduated doses on growing rats. J. Nutrition 10: 35-44.

        1935b. Studies of crystalline vitamin B. VI. The effect of graduated doses on pigeons. J. Nutrition 10: 161-6.

Watkins, W. E. and H. H. Mitchell. 1936. The phosphorus requirements of growing chickens, with a demonstration of the value of controlled feeding. Poultry Sci. 15: 32-41.

Weaver, E. M. F., J. D. Van Valkenburg, J. B. Stewart, A. D. McKinley, Jr. and C. Ermshar. 1947. Medical problems of long range fighter missions. A study in fatigue. J. Aviation Med. 18: 341-51; 398.

Welsh, J. H. and J. E. Hyde. 1944. Acetylcholine content of the myenteric plexus and resistance to anoxia. Proc. Soc. Exptl. Biol. Med. 55: 256-7.

Wetzig, P. and F. E. D'Amour. 1943. The effects of polycythemia and of a carrot diet on resistance to anoxia. Am. J. Physiol. 140: 304-7.

Whitehorn, W. V., A. Lein and A. Edelmann. 1946. The general tolerance and cardiovascular responses of animals to explosive decompression. Am. J. Physiol. 147: 289-98.

Whitehorn, W. V., A. Lein, A. Edelmann and F. A. Hitchcock. 1947. The effect of explosive decompression on cerebrospinal fluid pressure. Am. J. Physiol. 148: 253-8.

Whitehorn, W. V., A. Lein and F. A. Hitchcock. 1947. The effect of explosive decompression on the occurrence of intravascular bubbles. J. Aviation Med. 18: 392-4.

Whitehouse, A. G. R. 1931. Further investigation of sweating and sweat. Proc. Roy. Soc. (London) 108 B: 326-39.

        1935. The dissolved constituents of human sweat. Proc. Roy. Soc.(London) 117B: 139-54.

Wickson, M. E. and A. F. Morgan. 1946. The effect of riboflavin deficiency upon carbohydrate metabolism in anoxia. J. Biol. Chem. 162: 209-20.

Williams, O. L., W. R. Lyons, E. V. Bridge and S. F. Cook. 1946. The use of drugs for the prevention of decompression sickness. J. Aviation Med. 17: 602-5; 567.

Williams, R. D., H. L. Mason, R. M. Wilder and B. F. Smith. 1940. Observations on induced thiamine (vitamin B1) deficiency in man. Arch. Intern. Med. 66: 785-99.

Williams, R. R. (Editor) 1947. Appraisal of human dietaries by experiment. A conference held under the auspices of the Williams-Waterman Fund for the Combat of Dietary Diseases. New York: Williams-Waterman Fund Research Corporation, 130 pp.

Williams, R. J., M. A. Eppright, E. Cunningham and C. A. Mills. 1944. B vitamins in the tissues of rats maintained at high and low temperatures. Arch. Biochem. 5: 299-306.

Williamson, R. 1941. A note on the epidermis of the rat on a fat-free diet. Biochem. J. 35: 1003-5.

Wilmer, W. H. and C. Berens. 1918. Medical studies in aviation. V. The effect of aviation

on ocular functions. J. Am. Med. Assoc. 71: 1394-8.

Winslow, C.-E.A., A. P. Gagge and L. P. Herrington. 1939. The influence of air movement upon heat losses from the clothed human body. Am. J. Physiol. 127: 505-18.

Winslow, C.-E.A., L. P. Herrington and A. P. Gagge. 1937. Relations between atmospheric conditions, physiological reactions and sensations of pleasantness. Am. J. Hygiene 26: 103-115.

Wolff, R. and R. Karlin. 1947. La riboflavine hepatique et la résistance a l'anoxie chez la Souris. (Hepatic riboflavin and resistance to anoxia in the mouse.) Compt. Rend. Soc. Biol. 141: 772-4.

Wood, E. H., E. H. Lambert, E. J. Baldes and C. F. Code. 1946. Effects of acceleration in relation to aviation. Federation Proc. 5: 327-44.

Woodbury, R. M. 1942. Food consumption and dietary surveys in the Americas: Results-methods. Montreal, International Labor Office Report to the Eleventh Pan American Sanitary Conference held in Rio de Janeiro, September 7 to 18, 1942, 64 pp.

Woodruff, L. M. 1941. Survival of hypothermia by the dog. Anesthesiology 2: 410-20.

Wright, I. S. and E. MacLenathen. 1939. Excretion of vitamin C in the sweat. J. Lab. Clin. Med. 24: 804-5.

Yaglou, C. P. 1926. The thermal index of atmospheric conditions and its application to sedentary and to industrial life. J. Industrial Hyg. 8: 5-19.

_____ 1945. Note on the tolerance to various high levels of dry bulb temperatures and relative humidity. Naval Med. Res. Institute NH6-1/ALL/x-205, Q.M.C. Project x-205, August 14, 2 pp.

Yaglou, C. P. and P. Drinker. 1928. The summer comfort zone: climate and clothing. J. Indust. Hygiene 10: 350-63.

Youngburg, G. E. and M. W. Finch. 1926. The effect of temperature on metabolism, particularly that of protein. J. Biol. Chem. 68: 335-41.

Zook, J. and G. R. Sharpless. 1938. Vitamin C nutrition in artificial fever. Proc. Soc. Exptl. Biol. Med. 39: 233-6.

Zselyonka, L. and K. Nánássy-Megay. 1937. Ascorbic acid in human perspiration. Orvosi Hetilap 81: 800-1; Chem. Abs. 31: 7098, 1937.